THE CONNECTIONS OF THE PULVINAR

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THE CONNECTIONS OF THE PULVINAR

by

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This Thesis is dedicated to my father,

Prof. P. F. Cluver.

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INTRODUCTION

The name pulvinar thalami optici or "cushion" was given to the overhanging posterior portion of the thalamus of man by Burdach in 1822 (Polyak, 1955).

In the past much of our knowledge about the central nervous system has been obtained by correlating clinical with pathological findings (Lissauer, 1890; von Monakow, 1892; Bonhoeffer, 1897; Head and Holmes, 1911; Wilson, 1914; Papez, 1937; Simma, 1952; Cairns, 1952). Unfortunately the thalamus, especially the pulvinar, is a clinically silent structure insofar as there are no typical localising symptoms of a primary lesion of this nucleus (Yakovlev, 1969). Tumours of the pulvinar usually present with symptoms of pressure on neighbouring structures (Smythe and Stern, 1938), while vascular lesions are not normally restricted to this nucleus (Sheps, 1945). No metabolic disease specifically affects the pulvinar as is the case for instance with the lentiform nucleus in Wilson's disease. It is clear that, for a better understanding of the function of this nucleus, we have to depend on experimental work in the first place.

A striking feature of the evolution of the pulvinar among all the thalamic nuclei is its sudden development in primates. "The greatest phylogenetic elaboration of the thalamic structures

occurs in the pulvinar, which from an extremely rudimentary structure in rodents becomes the largest of thalamic nuclei in man." (Walker, 1966). As a result of this development the primate pulvinar differs considerably in size and complexity from the same nucleus in the cat, whereas a nucleus of a more constant size in phylogeny such as the ventro-postero-lateral nucleus shows a high degree of similarity in all these subjects. A study of the functional significance of the pulvinar, based on its connections with other centres, could benefit considerably from a comparative anatomical approach to the problem. The functional significance of a simple system is more readily understood and may serve as a basis for understanding the primate pulvinar.

Here, therefore, we have a thalamic nucleus which, although no primate prerogative, is certainly most developed in the higher primate and man. It is intimately related to the association cortex and appears from clinical observations to be associated with the receptive part of visual and oral communication. Unlike most other thalamic nuclei it apparently does not act as a relay station in any one of the afferent systems, although such a function in the visual system cannot be excluded at present.

Apart from the experimental work and clinical observations, there have also been speculations on its function. One such a speculation is that it serves as an integration centre for

visual and auditory information (Hassler, 1958). Another is that it has to do with the reproduction of "complex non-spatial time order functions of a symbolic configurational (Gestalt) nature" (Papez, 1939).

Despite all this, Walker as recently as 1966 stated at a symposium on the thalamus that: "It is thus apparent that the pulvinar is the terra incognita of the thalamus". There cannot be many better reasons for studying the connections of this nucleus.

The present investigation consists of three main sections, namely the retino-pulvinar projection (Chapter IV), the pulvino-cortical projection (Chapter V) and the cortico-pulvinar projection (Chapters VI and VII). Each section consists of an independent investigation in which different techniques and different species of animals were used. In the final discussion (Chapter VIII) the findings in the various chapters will be integrated.

The retino-pulvinar projection was studied because the existence of such a projection has been disputed by many authors. As the only afferent system which may be directly connected to the pulvinar, it is of major importance for our understanding of the function of the pulvinar to know whether or not such a connection exists.

Because of the lack of any specific study on the pulvino-cortical projection in subprimates this projection was studied in the cat, but a similar investigation was not undertaken in a primate as this projection has been extensively investigated in various primates.

The cortico-pulvinar projection was studied in the rhesus monkey. Because our findings were in many ways contradictory to those of other authors, who had however investigated this projection in the cat, an electron microscopical study of this projection was undertaken in addition to the light microscopical investigation.

CHAPTER I

REVIEW OF THE LITERATURE

I.1 The Evolution of the Pulvinar

On the basis of the phylogenetic development of the thalamus, its nuclei can be divided into three groups (Rose and Woolsey, 1949).

The first group consists of the paraventricular complex, the habenular complex and the pretectal nuclei. These are entirely independent of the endbrain. They are well developed in reptiles and birds where they form the largest part of the thalamus. These nuclei progressively diminish in relative size as one goes up the evolutionary scale.

Secondly, these authors recognise a dorsal thalamic group in which each nucleus has a projection to the endbrain. This group is subdivided into extrinsic or intrinsic nuclei depending on whether or not they receive a substantial portion of their afferents from extrathalamic sources. These authors maintain that the neocortex of primitive mammals consists largely of projection areas of extrinsic thalamic nuclei, or primary cortical areas. In higher forms the projection area of the intrinsic thalamic nuclei, the so-called secondary or association cortex, becomes dominant. The intrinsic thalamic nuclei, which become dominant in primates, are again subdivided

into those projecting to the neocortex, and those which are better developed in macrosømatic mammals, projecting to the rhinencephalon.

The third subdivision is the ventral thalamus, consisting of nuclei like the reticular nucleus which projects to a large cortical area. These nuclei remain relatively constant in size and are apparently related to cortical activation.

The pulvinar is classified as belonging to the intrinsic group of thalamic nuclei which project to the neocortex. This group consists of the "mediodorsal nucleus, the lateral and posterior nuclei and the pulvinar complex. All nuclei in these groups, although probably already present in opossum and certainly in rat and rabbit, are only modestly developed in these forms. The pulvinar in particular is quite minute. All of them increase markedly in relative size in ungulates and carnivores, and in the primates their development and internal differentiation reaches remarkable proportions." (Rose and Woolsey, 1949).

This classification has the virtue of illustrating two important aspects of the thalamic nuclei. In the first place there are some nuclei which have considerable survival value (to judge from their relative size) in one species, but may be insignificant in size (and presumably in their survival value) in another species. Other nuclei remain constant in

their relative size in different species. This suggests that functionally they are of equal importance in all species. Conclusions drawn from studies of the functional significance of nuclei of the latter group therefore should be applicable to all mammalian species.

This classification also illustrates that a nucleus develops or declines with the system of which it is part. It was recognised by von Monakow (1892) and Mann (1905) that the development of a thalamic nucleus is related to the development of the cortical area with which it is connected.

The first appearance of the pulvinar in the phylogenetic scale has not yet been established. Conflicting proposals have been made to this question. The reason for this controversy lies in the application by some authors of the name pulvinar to a particular region because of a similar position and cytoarchitectural appearance to the primate pulvinar, but without establishing whether the subprimate region so named had similar connections to the primate pulvinar.

Thus Grünthal (1934) came to the conclusion, in a purely cytoarchitectural study, that the pulvinar is a unique feature of the primate, after studying opossum, mouse, dog, rhesus monkey, chimpanzee and man. On the other hand, Le Gros Clark (1928, 1930) recognised a

pulvinar in the primitive insectivore, Tupaia minor, as well as a distinctly developed pulvinar in Tarsius, which is regarded as the most primitive of all primates. He further became convinced that the pars posterior of the lateral nucleus of the rat is a homologue of the primate pulvinar, and concluded that: "It thus appears that far from being a prerogative of the primates, the pulvinar is a common mammalian feature." (Le Gros Clark, 1930).

This latter view was also shared by Ingvar (1923), Kappers Huber and Crosby (1936), and Rose and Woolsey (1949), whose opinions were also based on the relative position and cyto-architectural appearance of the nuclei compared.

Tsai (1925) and later Toncray and Krieg (1946) went even lower in phylogeny and proposed that the pretectal nucleus of the opossum and other lower animals can be regarded as a homologue of the primate pulvinar. This is most unlikely as it has been shown that both the pulvinar and the pretectal nucleus are present in lower primates (Le Gros Clark, 1932). Furthermore, lemniscal fibres are known to terminate in the pretectal nucleus in subprimates and primates, but have never been shown to terminate in the pulvinar (Le Gros Clark, 1932; Kappers, Huber and Crosby, 1960). Recently this finding was confirmed by Lund and Webster (1967) who were able to demonstrate degeneration by the Nauta method in the pretectal nucleus after lesions in the gracile and cuneate nuclei, while no degener-

ation was seen in the pulvinar in the same animal.

In 1945, Grunthal studied the thalamocortical projection of the mouse and found that the region of the thalamus proposed by some as the homologue of the primate pulvinar did not project to the cortex at all. Because of the intimate relation of the primate pulvinar with the cortex (Mann, 1905; Le Gros Clark and Northfield, 1937; Walker, 1938b; Bucy and Klüver, 1940), Grünthal regarded this as conclusive proof that the mouse has no nucleus comparable with the primate pulvinar.

A large pulvinar in proportion to the rest of the thalamus is generally recognised in the cat on cyto-architectural grounds (Ingram, Hannet and Ranson, 1932; Jiménez-Castellanos, 1942; Jasper and Ajmone-Marsan, 1954; Reinoso-Suàrez, 1961). The cat pulvinar does project to the cortex, and as far as this projection has been studied, it is comparable with the projection of the primate pulvinar (Waller and Barris, 1937; Sprague, 1966; Wilson and Cragg, 1967).

From the literature it is apparent that although a structure resembling the pulvinar is recognised in some subprimates, it is by no means clear whether this nucleus is a true homologue of the primate pulvinar.

There is no doubt that the development of the pulvinar is related to the development of the association cortex at the junction of the occipital temporal and parietal lobes (Aarenson and Papez, 1934; Kappers, Huber and Crosby, 1936; Walker, 1937; Sheps, 1945; Toncray and Krieg, 1946; Hassler, 1959). There is some disagreement however on the exact demarcation of the cortical region related to the pulvinar in phylogeny. According to Kappers, Huber and Crosby (1936), the development of the pulvinar goes "hand in hand in relation to the visual association cortex, in the same manner as the lateral thalamic nucleus develops with the parietal and other cortical association areas". Other authors believed that the pulvinar is related to the cortex anterior to Area 19 (Aarenson and Papez, 1934; Walker, 1938; Sheps, 1945; Hassler, 1959).

The position regarding the cortical projection of the pulvinar is well summed up by Walker (1938). "The pulvinar has a wide projection to an area of cortex which lies along the anterior margin of Area 19. This is the cortex which has been previously mentioned as cytoarchitecturally transitional, a fact which is apparent not only from direct histological examination of the cortex, but also from the fact that no two authors agree as to the precise borders of the cytoarchitectural areas in this region. It must be further emphasised that it is this region which is undergoing

marked elaboration in phylogeny, attaining its acme in the supramarginal and angular gyri of the human cerebral cortex."

I.2 The Subdivisions of the Pulvinar

The pulvinar occupies the caudal end of the dorsal thalamus. The nucleus is subdivided on a topographical basis. This presents some difficulty as the nucleus is a fairly uniform structure. Topographical differences have therefore to be used, as Olszewski (1952) stated "- as far as they present themselves".

Table I summarises the various classifications of the pulvinar reviewed below. The pulvinar is subdivided into three parts, lateral, medial and inferior, according to the classifications of Crouch (1934), Walker (1938), Sheps (1945) and Chow (1950). The last author was also able to demonstrate that these subdivisions of the pulvinar project to different cortical regions, so giving a functional basis for this classification. An additional oral division (Table I.1c) was later recognised by a number of authors (Olszewski, 1952; Dekaban, 1953; Crosby, Humphry and Lauer, 1962). This subdivision into four parts is generally accepted and seems to be justified functionally from the work of Chow (1950) and Locke (1960). It only holds good however in the simian. A similar subdivision is not possible in, for instance, the cat where the pulvinar is not clearly demarcated and not subdivisible on topographical

grounds (Ingram, Hannet and Ranson, 1932).

There exist a number of classifications which differ from this in a greater or lesser degree and should therefore be mentioned. Friedemann (1913) subdivided the pulvinar into medial and lateral parts (Table I.1A) which were again further subdivided as follows:

Lateral pulvinar:	p mu
	p eta
Medial pulvinar:	p epsilon
	p delta
	p gamma
	p alpha

In this classification the lateral pulvinar is comparable with that of Crouch (1934), Walker (1938), Sheps (1945), and Chow (1950), and the medial pulvinar, except for its subdivision p delta, comparable with their medial pulvinar. The subdivision p delta then represents their inferior pulvinar.

The classification of Grünthal (1934) is considerably more complicated insofar as he subdivided the pulvinar into different parts in various simians and man (Table I.1E, F and G). In the Macaca mulatta the pulvinar is subdivided into four nuclei: p^1, p^2, p^3, and griseum intergeniculatum. In the chimpanzee it is subdivided into three nuclei: the medial pulvinar named "p", nucleus semilunaris and griseum inter-

geniculatum. In man the pulvinar is subdivided into five nuclei, p^1, p^2, p^3, p^4 and griseum intergeniculatum. It should be noted that Grünthal regards the nucleus semilunaris as part of the pulvinar in the chimpanzee, but not in man in whom it is completely unrelated to the pulvinar. Furthermore, the nuclei p^3 and p^4 have no homologue in the chimpanzee and are looked upon as being a prerogative of man.

In his classification of the human pulvinar, Hassler (1958) recognised a nucleus pulvinaris superficialis in addition to the generally accepted lateral, medial, ventral (inferior) and oral subdivisions (Table I.1 D). These are further subdivided as follows:

Nucleus	Subdivisions
Nucleus pulvinaris superficialis	None
Nucleus pulvinaris lateralis	1. Pars pulvinaris lateralis superior
	2. Pars pulvinaris lateralis inferior
Nucleus pulvinaris medialis	1. Pars pulvinaris medialis internus
	2. Pars pulvinaris medialis dorsalis
	3. Pars pulvinaris medialis centralis
	4. Pars pulvinaris medialis ventralis
Nucleus pulvinaris ventralis	1. Pars pulvinaris intergeniculatus
	2. Pars pulvinaris suprabrachialis
Nucleus pulvinaris oralis	1. Pars pulvinaris orolateralis
	2. Pars pulvinaris oromedialis
	3. Pars pulvinaris oroventralis

Certain points of difference between these classifications should be emphasised. The griseum inferior of Grünthal (1934)

was accepted as equivalent to the n. pulvinaris inferior of the other classifications. It is however possible that p^2 and p^3 of Grünthal, if grouped together and considered to represent the medial pulvinar of other authors, may include slightly more or less than the medial nucleus of Crouch (1934) and others.

In the case of the human pulvinar, the subdivision has been made on a cytoarchitectural basis and it is therefore difficult to decide whether it has any subdivisions which have no homologue in simians as was claimed by Grünthal (1934) and Hassler (1958). The classification of the pulvinar into lateral, medial, inferior and oral parts will be used throughout the present investigation as this is not only based upon cytoarchitectural differences (Olszewski 1952, and others), but also has a functional basis insofar as these divisions project to different cortical areas in the simian (Chow, 1950; and Locke, 1960).

I.3 Connections of the Pulvinar

(a) Afferent Connections

Little is known about the afferent connections of the pulvinar. The best known, but also the most disputed, afferent connection is that with the retina. A small projection from the superior colliculus has been described. At present the most important afferent connection appears to be with the temporal and possibly the occipital cortex.

Table I.1 SUBDIVISIONS OF THE PULVINAR

Authors	Species	Subdivisions
A. Friedemann 1913	Cercopithecus	1. Lateral 2. Medial
B. Crouch 1934 Walker 1938 Sheps 1945 Chow 1950	Macaca) Macaca) Homo) Macaca)	1. Lateral 2. Medial 3. Inferior
C. Olszewski 1952 Delnaban 1953 Crosby, Humphry & Lauer 1962	Macaca) Homo)) Homo)	1. Lateral 2. Medial 3. Inferior 4. Oral (part of lateral)
D. Hassler 1958	Homo	1. Lateral 2. Medial 3. Inferior 4. Oral (part of lateral) 5. Superficial (no homologue)
E. Grünthal 1934	Macaca	1. p^1 (lateral) 2. p^2) 3. p^3) (medial) 4. griseum intergeniculatum (inferior)
F. Grünthal 1934	Pan	1. nucleus semilunaris (lateral) 2. p (medial) 3. griseum intergeniculatum (inferior)
G. Grünthal 1934	Homo	1. p^1 (lateral) 2. p^2 (medial) 3. p^3) 4. p^4) (no homologue) 5. griseum intergeniculatum (inferior)

(i) Retina

Because of its immediate proximity to the lateral geniculate nucleus the pulvinar was often grouped with the lateral geniculate body and superior colliculus as a primary optic centre (Minkowski, 1920). The termination of retinal fibres in the pulvinar has been described by a number of authors (Probst, 1900; Minkowski 1920; Cajal, 1955; Hassler, 1959, 1960, 1965; Altman,1962). It is interesting to note that Minkowski (1920) was able to demonstrate degeneration in the pulvinar after eye-enucleation in rabbits and goats, but no degeneration was seen in the pulvinar of macacus rhesus and two human cases in his series.

"Beim Affen und Menschen konnte ich einen Unterschied zwischen beiden Pulvinaria nach Enukleation eines Auges nich feststellen; indessen glaube ich doch, im Anschluss an eigene Befunde an niederen Tieren und von jene anderen Autoren am Menschen, dass auch bei diesen Sehnervenfasern in Pulvinar endigen." (Minkowski, 1920).

On the other hand there are many authors (Gudden, 1885; Brouwer, 1923; Brouwer and Zeeman, 1925 and 1926; Le Gros Clark, 1932; Barris, Ingram and Ranson, 1935; Heyhow, 1958 and 1967; Heyhow et al., 1962; Laties and Sprague, 1966) who have shown that optic fibres pass through the pulvinar on their way to the superior colliculus, but

that these do not terminate in the pulvinar. Because of this contradictory evidence, one cannot regard the problem of a possible retinal projection to the pulvinar as finally solved.

(ii) Superior Colliculus

Altman and Carpenter (1961) were able to demonstrate a projection from the superior colliculus to the caudal part of the pulvinar in cats. This projection was studied with the Nauta-Gygax technique after stereotaxically placed lesions in the superior colliculus.

(iii) Cerebral Cortex

A temporo-pulvinar projection, arising from the pyriform cortex and amygdala, was described by Papez (1937) in Macaca mulatta. Further evidence of an afferent connection from the temporal lobe was presented by Bucy and Klüver (1955) who demonstrated the presence of a large bundle of degenerated fibres terminating in the pulvinar after temporal lobectomy. Detailed studies on the temporo-thalamic projection were done by Whitlock and Nauta (1956) using the Nauta method, and by Stoll, Marsan and Jasper (1951), and Jasper, Marsan and Stoll (1952) by electrophysiological methods. They were able to show that the pulvinar receives

fibres from all three temporal gyri as well as the tip of the temporal lobe. The weight of later evidence therefore suggests that the temporal projection arises mainly from temporal neocortex and not from the pyriform cortex and amygdala as suggested by Papez (1937). This cortico-fugal projection appears to reciprocate with the pulvino-temporal projection described by Chow (1950).

The possibility of a projection from the occipital cortex to the pulvinar had been mentioned by Edinger (1893), and Hitzig (1903). A projection from the lateral and posterolateral gyri (areas 17 and 18) to the pulvinar and n. posterior of the cat was described by Altman (1962) who removed the superficial cortex by suction and studied the resulting anterograde degeneration by the Nauta method. Majorossy, Réthelgi and Széntagothai (1965) stated that abundant degeneration was visible in the pulvinar after lesions involving the occipital cortex.

A projection from area 17, as well as from areas 18 and 19 to the inferior lateral divisions of the pulvinar of Galago crassicaudatus was demonstrated by Campos Ortega (1968).

Sachs (1909) found degeneration in the pulvinar of

cats after a lesion involving the anterior part of gyrus lateralis and gyrus suprasylvius (cat 99 of his series) and after a lesion of the posterior ectosylvian gyrus (cat 151). This area (posterior ectosylvian) was regarded as a secondary acoustic area (Ades, 1943).

A projection from the anterior lateral and suprasylvian gyri to the pulvinar in cats was also described by Niemer and Jiminez-Castellanos (1950) who looked upon this as "associational cortex".

(b) Efferent Connections

The afferent connections to the pulvinar, as far as they are known, come mainly from the cortex, the efferent projection of the pulvinar appears to be exclusively to the cortex. This conclusion was arrived at first by Walker (1935) who found the ipsilateral pulvinar to be completely degenerated in Macaca mulatta after hemi-decortication. This was confirmed in man by Powell (1952) who studied the thalamus of a patient who had died one month after a hemispherectomy had been performed. Murphy-Combs (1965) who studied newborn as well as young adult Macaca mulatta after hemi-decortication with a postoperative survival of from 15 to 31 days, found the pulvinar completely degenerated, except for the medial border of the inferior pulvinar in the infants. In one adult specimen however

the medial and ventral border of the pulvinar contained nearly 50% of normal neurons.

"It has been recognised from the time of von Monakow and Cajal that the different parts of the thalamus are projected on to areas of the cortex which occupy relatively similar positions." (Le Gros Clark, 1932).

This implies that fibres from the anterior part of the thalamus project to the frontal cortex and that those from the posterior part (i.e. pulvinar) project to the occipital lobe. In accordance with this concept of rostrocaudal topographical correspondence between thalamus and cerebral cortex the pulvinar will be expected to project predominantly to the posterior neocortical areas.

(1) Projection to the Occipital Lobe

Retrograde degeneration of the inferior pulvinar (p delta) and the lower part of the lateral pulvinar (p eta) after removal of the dorsal half of areas 18 and 19 in Macaca mulatta was described by Le Gros Clark and Northfield (1937). Walker (1938a) found retrograde degeneration in the lateral and inferior pulvinar after occipital lobectomy in the chimpanzee. It should be noted that although the degeneration was most severe in

the inferior pulvinar, a small strip of cells along its inferior and medial margin was left unaffected. This is in accordance with the findings of Peacock and Murphy-Combs (1965).

Chow (1950) in his study on the projection of the pulvinar in the Macaca mulatta found that the posterior ventral part of n. pulvinaris lateralis projected to the temporo-occipital region, whereas the dorsal half of the inferior pulvinar projected to the dorsal, and the ventral to the ventral prestriate cortex. These results were confirmed in the human by Hartmann and Simma (1952). According to Hassler (1965) the (intergeniculate) inferior pulvinar nucleus projected to area 18, and other nuclei of the pulvinar (presumably the lateral nucleus) projected to area 19. It is this latter system (area 19 - lateral pulvinar) which Hassler (1965) stated was affected in the case of "pure"alexia described by Beringer and Stein (1930) and which was anatomically examined by Hassler (1954).

(ii) Parietal Projection

It seems to be mainly the lateral pulvinar which projects to the parietal cortex (Le Gros Clark and Northfield, 1937; Walker, 1938a and 1938b; Chow, 1950; Hartmann and Simma, 1952). The most detailed

description was given by Chow (1950) who found the antero-dorsal part of the lateral pulvinar to project to the medial surface of the parietal lobe and to the posterior part of the superior parietal lobule. He found the anterior ventral part projected to the inferior parietal region.

(iii) Temporal Projection

There is an abundance of evidence in the literature supporting the presence of a pulvino-temporal projection. One is therefore at first somewhat surprised at the categorical denial by Simma (1954) of the existence of such a projection. "Die temporale Rinde hat, worauf wir bereits früher einmal hingewiesen haben, mit Ausnahme der Hörregion keine thalamischen Verbindungen." This opinion however is not as contradictory to the literature as would at first appear. Hartmann and Simma (1952) and Simma (1954) did in fact demonstrate the presence of a large projection from the pulvinar to the posterior part of the temporal lobe, but this area was classified as parietal cortex by them, because of its cytoarchitecture. In their cases in which the lesion was restricted to the anterior temporal lobe no thalamic degeneration was seen. A reason for this could be that the area affected by the lesion receives a sustaining type of projection from the thalamus (Rose and Woolsey, 1949). Under

these circumstances the resulting retrograde degeneration would be minimal or nonexistent.

Le Gros Clark (1936), in studying the thalamic connections of the temporal lobe, concluded that the main element of the pulvinar (p beta; n. pulvinaris medialis) projects to the posterior sylvian receptive region of Polyak, which extends backwards from the auditory area along the walls and lips of the sylvian sulcus as far as its caudal extremity.

After ablation of the superior and middle temporal gyri of the chimpanzee, Walker (1938a) found retrograde degeneration in the pulvinar stretching from its posterior pole forwards, involving part of pulvinar medialis and more anteriorly the inferior pulvinar. In a similar experiment in Macaca mulatta where only the tips of the three temporal gyri were left intact, Walker (1938b) found the pulvinar to be completely degenerated except for a caudal part of the n. pulvinaris medialis. This is contrary to the finding of Le Gros Clark (1936) who maintained that the pulvinar does not project to the temporal lobe anterior to the auditory area. It is interesting that the part of the medial pulvinar which remained intact in Walker's (1938b) experiment, was the same which degenerated in the experiment of Bucy and

Klüver (1955) after removal of the tip of the temporal lobe. Chow (1950) found that the posterior part of n. pulvinaris medialis projected to the tip of the temporal lobe, thus confirming the finding of Walker (1938b). Complete temporal lobectomy in the Macaca mulatta(Bucy and Klüver, 1940) partially affected the medial, lateral and inferior divisions of the pulvinar.

Simpson (1952), in experiments on Macaca mulatta and in a study of a human case with a temporal lesion, found that the medial pulvinar showed partial degeneration after lesions involving the superior temporal gyrus and near complete degeneration if the lesion involved the complete insular cortex and lips of the sylvian sulcus.

A very interesting idea has been brought forward by Locke (1960) to account for the projection of the medial pulvinar to the temporal lobe. He proposed a rostrocaudal rotation through 180° as well as a medial rotation of 90° by the medial pulvinar to explain the topographic organisation of this projection. This hypothesis is in full agreement with the findings of Chow (1950) and Bucy and Klüver (1955).

I.4 Clinical Pathological Studies

The use of pathological conditions to elucidate the functional anatomy of the central nervous system has been approached in two distinct ways.

The first method uses the hypothesis that a disease selectively affects a particular neural system because it is physiologically distinct from others. Should this be the case, we could expect a particular disease to cause a more or less constant pattern of symptoms related to the destruction of that system. This is described by Vogt and Vogt (1928) as follows: "Die häufige Beschränkung einer Erkrankung auf eine bestimmte topistische Einheit und das Nichtgetroffensein der benachbarten drängt uns zur Annahme irgendeiner physiologischer Differenz zwischen den erkrankten und den intakt gebliebenen nervösen Elementen." Tabes dorsalis and Wilson's disease are conditions which seem to conform to this hypothesis. Lissauer (1890) described degeneration in the pulvinar in cases with progressive paralysis. One of these cases had a sensory aphasia without other clinical neurological manifestations and in this case degeneration was confined to the medial pulvinar. Another case had sensory involvement of the right hand as the only symptom, and degeneration was found in the lateral pulvinar. According to Schultz (1898) cases with advanced progressive paralysis had complete atrophy of the pulvinar at post mortem.

Sciati (1907) reported the presence of degeneration in a number of thalamic nuclei in dementia paralytica. In all his cases the degeneration was, however, most pronounced in the pulvinar. Much later Simma (1951) extensively investigated thalamic changes in progressive paralysis. He concluded that degenerative changes in the pulvinar are not due to a primary attack of the disease on this nucleus, but rather the result of retrograde degeneration secondary to cortical involvement. The reason for the pulvinar being so commonly affected is because the parietal and occipital cortex, to which this nucleus projects, is especially involved in this condition (Simma, 1951). Progressive paralysis therefore does not fall into the category described by Vogt and Vogt (1928) as far as the pulvinar is concerned.

This approach has therefore clearly not helped our understanding of the functional significance of the nucleus very much. Other workers did not hold the above view and used clinical material as "experiments of nature" in an attempt to learn more about the function of the pulvinar. In this second method the lesions produced by any of a variety of pathological conditions are studied as naturally occurring disruptions of the anatomy and function of this nucleus.

(a) Clinical Evidence of Retinal Connections

Minkowski (1920) studied the course and termination of

the optic tract in man and a number of animals. He failed to find any evidence of a retino-pulvinar projection in man, but remained convinced of its existence on the grounds of its presence in cats and goats investigated by him.

Hassler (1965) described a case of anophthalmia in a patient in whom extreme hypoplasia of the inferior pulvinar was seen at post mortem.

(b) Clinical Evidence of Cortical Connections

Von Monakow (1892) described three cases with lesions of the parieto-occipital cortex. The important common features in these cases were the concomitant presence of a cortical lesion extending from the visual area forwards to include the angular gyrus, degeneration of the pulvinar affecting its lateral part, and symptoms of homonymous hemianopia, receptive aphasia and alexia.

Papez (1937) described a number of cases with lesions involving the temporo-parieto-occipital area. In all cases aphasia was present and the pulvinar was severely degenerated. Other thalamic centres were involved inconstantly to varying degrees. He concluded that:
"From numerous verified cases of aphasia it seems that the functions of perception are seriously affected by

diseases of the temporal, occipital and parietal association areas. When in addition the pulvinar and its connections are involved, more serious mental disorders and deficiencies occur."

In a clinico-pathological study of a number of cases with thalamic tumours, Smythe and Stern (1938) described a patient presenting with symptoms of childishness and fatuousness followed by aphasia, alexia and agraphia. At a later stage a right hemiparesis, hemianaesthesia and iridoplegia developed. At post mortem an astrocytoma, involving mainly the left pulvinar, was found.

Sheps (1945) described three cases of thalamic degeneration following cortical lesions. One had general cortical degeneration, the second case degeneration in the area of distribution of the middle cerebral artery, and in the third case the degeneration was confined to the frontal and insular cortex. Degeneration of the pulvinar was seen only in the first two cases. From this it appears that the pulvinar does not project to the insula or frontal cortex.

Hartmann (1943) studied two cases with Pick's disease. From these he concluded that most of the pulvinar projects

to Area 19 except its anterior (oral) part which projects to the angular gyrus (Area 39). A similar conclusion was reached by Simma (1951) who studied retrograde degeneration of the thalamus in cases with senile dementia and Alzheimer's disease. In further clinico-pathological investigations Simma (1952a, 1952b and 1954) described a number of cases with sensory aphasia, cortical lesions in the parieto-occipito-temporal area and retrograde degeneration in the pulvinar. In most of these cases the cortical pathology was rather extensive and the degeneration therefore not confined to the pulvinar.

1.5 Methodology

This review is not strictly limited to the methods used in this investigation, but also includes some of the methods frequently referred to in the course of this paper. Special emphasis has been laid on the criteria for the recognition of degeneration with the various methods.

(a) Types of Degeneration

The cutting of an axon can have the following consequences (see fig. I.1). Firstly degeneration of the axon distal to the lesion or so-called anterograde or Wallerian degeneration occurs. Secondly there occurs degeneration of the axon proximal to the lesion including

the neuron from which it arises. This is known as "retrograde" degeneration. Finally the neuron, on which the degenerated axon terminates, may also degenerate. This process is known as transneuronal degeneration. It is generally assumed that these different types of degeneration occur in the chronological sequence in which they have been mentioned above.

(i) Anterograde Degeneration

That the distal portion of a severed nerve fibre undergoes degeneration, was first observed by Türck (1851) and Waller (1852). The axoplasm of the distal isolated fibre undergoes fragmentation and droplet formation. According to the theory of Young (1945), the cell body does not only produce axoplasm, but also maintains it under constant pressure, which is normally sufficient to hold the axoplasm in the form of a tube against the force of the surface tension. When the fibre is cut, the pressure in the axoplasm is released and it rapidly fragments. The axoplasm is later phagocytosed by oligodendroglia. At a later stage the myelin sheath starts to fragment and it is also phagocytosed by oligodendroglia. In the terminal area (fig. I.1) the process can follow one of two different courses

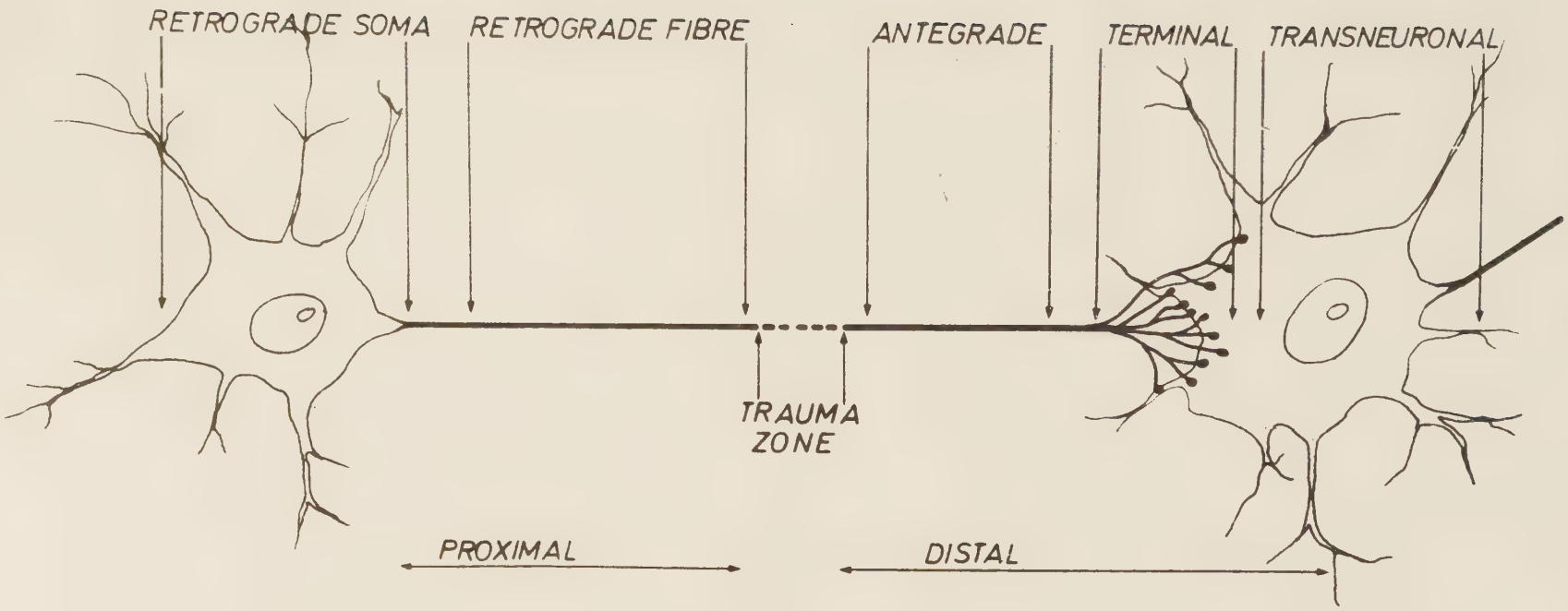

RETROGRADE SOMA
RETROGRADE FIBRE
ANTEGRADE
TERMINAL
TRANSNEURONAL
TRAUMA ZONE
PROXIMAL
DISTAL

Fig. I.1.

(Gray and Guillery, 1966). These are either a fibrillary hypertrophy, as is seen in the terminal boutons of retinal fibres in the lateral geniculate body, or "dark", necrotizing type of degeneration. The latter develops quicker than the former. The necrotizing type of degeneration is, for instance, found in the tectum after eye enucleation.

(ii) Retrograde Degeneration

This refers to the degeneration proximal to the lesion, involving both the soma and the axonal stump.

1. Degeneration of the Soma

This was described by Nissl (1892) and consists of chromatolysis, shrinkage and in some cases disappearance of the cell, following damage to the axon. It varies greatly in different parts of the central nervous system. This reaction can be reversable, that is, following the acute stage of tigrolysis and chromatolysis, the cell nucleus does not degenerate, but forms new chromatin bodies in superabundance. This occurs in the dentate nucleus after section of the superior cerebellar peduncle (Walker and Botterell, 1937). In the thalamus however, the acute stage of chromatolysis is usually followed by nuclear degener-

ation, but even within the thalamus there exist differences between individual nuclei (Walker, 1938b). Further it is well established that the closer the lesion is to the soma, the more severe is the degree of chromatolysis and tigrolysis (Van Gehuchten, 1903). If an axon has a number of collateral branches, most or all of these, or the main axon, have to be damaged before the soma of the neuron will degenerate. Should each neuron of a nucleus not only project to a particular cortical area but also send a collateral fibre to an adjacent area (sustaining projection) (Rose and Woolsey, 1948) then a lesion small enough not to damage the collateral will not result in degeneration of the soma. If however a cortical area receives an exclusive projection from a particular neuron (essential projection) (Rose and Woolsey, 1948), ablation of this area will result in retrograde degeneration of the neuron concerned.

2. Degeneration of the Axonal Stump

This is also known as fibrillar retrograde degeneration or indirect Wallerian degeneration (Crosby, Humphrey and Lauer, 1962; Beresford, 1965). The term indirect Wallerian degeneration was first used by Van Gehuchten (1903) when he observed that the process was similar to true Wallerian degeneration.

This process of retrograde axonal degeneration can be observed to start in the soma and progress centrifugally along the axonal stump (Van Gehuchten, 1903; Glees, Soler and Bailey, 1951; Cowan, Adamson and Powell, 1961). It is therefore clear that "retrograde" degeneration involving the axon proximal to the lesion is no different in its appearance from "anterograde" degeneration, involving the axon distal to the lesion. The only difference between these two "types" of degeneration is that the process occurs somewhat earlier in the distal than in the proximal axon (Beresford, 1965).

(iii) Transneuronal Degeneration

The cells affected by this condition do not properly degenerate, but enter a permanent state of atrophy (Walker, 1938b). This is not the result of damage to the particular neuron, but caused by deafferentation. Transneuronal degeneration occurs in some parts of the central nervous system only, for instance the lateral geniculate body after eye enucleation.

(b) Methods for Demonstrating Degeneration

(i) Anterograde Degeneration

This can be demonstrated by light microscopy with

the methods of Marchi (1885), Weigert (1897) and Bielschowsky (1904), or their modifications.

1. The Marchi Method

The Marchi method was the first histological technique which allowed selective impregnation of degenerated fibres. It is the method of classical neuroanatomy, and the one used for establishing most of the neuroanatomy set out in current textbooks (Bowsher, Brodal and Walberg, 1960). This method only stains degenerated myelin and can therefore be employed even after a considerable post-operative survival period. It is, of course, incapable of demonstrating either degenerated unmyelinated fibres or the terminal part of myelinated fibres. According to Marion Smith (1956) the occurrence of artifacts which are indistinguishable from true degeneration is the most serious disadvantage of this method.

2. The Weigert Method

The Weigert method, and its numerous modifications, selectively stains myelin. It is therefore used in classical neuroanatomy for demonstrating the absence of certain pathways, for instance the posterior columns in Tabes dorsalis (Crosby, Humphry and Lauer,

1962). This is obviously not a method which allows great accuracy.

3. The Silver Methods

At the beginning of this century the reduced Silver techniques, or neurofibrillar methods of Cajal (1904) and Bielschowsky (1904) were developed, and used to demonstrate normal nerve fibres. The first person to employ the Cajal impregnation principle for the demonstration of degenerated boutons terminaux was Hoff (1932). Since that time a number of silver techniques, better suited for the demonstration of degenerated fibres have been developed. Those most commonly employed are based upon the Bielschowsky principle of frozen section impregnation. The method however has the disadvantage of concomitantly staining normal fibres as well.

In 1946 Glees developed a modification of the Bielschowsky technique which was capable of impregnating actual termination sites of degenerated axons.

Somewhat later Nauta (1950) developed another modification of the Bielschowsky technique which is known as the "original" or "non-suppressive" Nauta method (Nauta, 1950; Nauta and Gygax, 1951), in which

no attempt was made to suppress the impregnation of normal fibres. This is therefore a fundamentally different method from the later developed Nauta-Gygax method in which suppression of normal fibres was achieved by the introduction of phosphomolybdic acid and potassium permanganate pretreatment (Nauta and Gygax, 1954). This suppressive Nauta-Gygax method was later modified by replacing the ammoniated silver nitrate solution with ammoniated silver carbonate solution of Laidlaw as suggested by Chambers, Liu and Liu (1956) and after this also advocated by Nauta (1957). This method is widely used to demonstrate degenerated fibre pathways as well as their terminations, as it allows the selective impregnation of degenerated nerve fibres as well as a fair proportion of the degenerating axon terminals. The suppression of the impregnation of fibres is however obtained at the expense of a considerable reduction in the number of degenerating axonal terminals impregnated (Heimer, 1966). In order to obtain a more consistent impregnation of fine terminal fibres and synaptic thickenings, a modification of the original "non-suppressive" Nauta method was developed by Fink and Heimer (1967).

These selective silver methods have the advantage

over the Marchi method in that they impregnate the axoplasm instead of the myelin sheath, and therefore demonstrate unmyelinated and terminal axonal aborizations, which could not be seen with the Marchi method. Further, compared with the Marchi method, the Nauta method has the advantage that artifacts are more easily distinguished from true degeneration (Evans and Hamlyn, 1956; Bowsher, Brodal and Walberg, 1960).

The suppressive Nauta method allows degenerated fibres to be followed with far greater ease than does the Glees method, which is however superior when exact information on the termination of axons is required (Bowsher, Brodal and Walberg, 1960). The difference between the Glees and suppressive Nauta methods in demonstrating axonal termination is not as great as it would seem from the terms "terminal" and "preterminal" degeneration. These terms are commonly used to distinguish between the types of degeneration demonstrated by each of these methods respectively at the terminal part of the fibre.

The term "terminal degeneration" for the changes seen at synaptic endings with this method was suggested by Glees (1946). According to Evans and Hamlyn (1956)

the suppressive Nauta methods impregnated a lipid which is present in too small amounts in synaptic endings to allow their demonstration. The term "preterminal degeneration" was therefore used for the pericellular aborizations seen in the "suppressive" Nauta-Gygax method. It has become clear from electron microscopical studies of silver impregnated material (Walberg, 1964; Heimer and Peters, 1968), that all commonly used reduced silver methods can impregnate degenerated synaptic endings as well as fibres. Because we are often unable to determine the nature of a single argyrophylic body, the unqualified terms "preterminal " and "terminal" degeneration in relation to silver techniques seem unjustified (Walberg, 1964; Heimer, 1967). It is more appropriate to use the term "terminal degeneration" for the degeneration of both the axon aborizations and their synaptic endings as suggested by Nauta (1950), Sprague and Ha (1964), and Heimer (1967).

4. Criteria for the Recognition of Anterograde Degeneration with Silver Methods and Electron-Microscopy

The Glees Method

This method can reveal degenerated boutons in certain parts of the central nervous system,

as for instance the lateral geniculate body after eye enucleation. In these particular regions the degenerated terminal boutons swell up considerably and can be recognised without difficulty, as they have the appearance of large dark clubs. The survival period is very important because the degenerated boutons disappear while the degeneration of fibres is still developing. This makes it difficult to demonstrate both terminal degeneration with the Glees method and degenerated fibres with the Nauta method in the same animal (Glees and Nauta, 1955). The optimal survival period for the demonstration of degenerated boutons differs from species to species and also from one part of the central nervous system to another. In regions where the terminal boutons do not swell up during degeneration it is rather difficult to distinguish degenerated boutons from normal impregnated boutons. In these regions we have to rely on the following criteria (Bowsher, Brodal and Walberg, 1960):

(a) A large number of boutons in an area in which boutons are not visible in Glees sections of control material.

(b) A solid black appearance in an area where normal boutons have a ring-shaped appearance in Glees

stained control material.

(c) An irregular outline to the boutons is suggestive of degeneration.

(d) The presence of a tail to the bouton, especially if this tail connects the bouton to a degenerated fibre.

It is not yet clear which structures are responsible for the argyrophylia in a degenerating bouton. According to Gray and Guillery (1966) and Gray and Hamlyn (1962), the silver is deposited onto the neurofilaments. Walberg (1964) however showed that the argyrophylia of normal boutons in the inferior olive of the cat does not depend upon the presence of neurofilaments. More recently Heimer (1967), in an electron microscopical study of silver impregnation methods, was able to show that degenerating boutons in the olfactory cortex lack filaments, whereas they appear as solid black dots in Glees sections.

The Nauta Method

When we refer to the "Nauta method" we mean the suppressive Nauta method (Nauta, 1954), modified

according to Chambers, Liu and Liu (1956).

As is the case with the Glees (1946) method, the problem of argyrophylia has also not been solved in the Nauta method. According to Eager and Barnett (1966), who examined Nauta-stained material electron microscopically, the silver particles were seen mostly within the axoplasm. Frequently the myelin sheaths also contained silver deposits. These authors believed that the membraneous structures of the axoplasm as well as an accumulation of lipid, is responsible for the argyrophylia of degenerating axons.

According to Nauta (Glees and Nauta, 1955), droplike disintegration is the sole dependable criterion of axonal degeneration. Being a suppressive method, one could expect the degenerated fibres to be stained selectively, but unfortunately this is not the case. A varying number of normal fibres are always stained, although the degree of argyrophylia is greater in degenerated than in normal fibres. In the stage prior to disintegration, degenerating axons display local swellings, which can be difficult to distinguish from varicosities in normal axons. A further important

criterion is the extremely irregular appearance of the degenerated fragments (Bowsher, Brodal and Walberg, 1960).

The optimum survival time necessary for the demonstration of degeneration with the Nauta method varies from species to species and from one fibre system to another. For instance, most corticofugal fibres will degenerate to the stage of droplike disintegration within five days in the rat and the cat, but in the monkey appear to require more than seven days to deteriorate to the same stage (Glees and Nauta, 1955).

The Fink-Heimer Modification

This modification of the original non-suppressive Nauta method allows an enhanced argyrophylia of degenerated fibres while suppressing normal fibre impregnation, but to a lesser degree than the suppressive Nauta method (Fink and Heimer, 1967). Unlike the suppressive Nauta method, this modification does not impregnate the degenerated myelin sheath. Silver deposits are localised only in the axoplasm of the fibres and in the boutons terminaux, according to electron microscopical studies (Heimer, 1967).

This method is therefore less effective than the suppressive Nauta method for tracing fibre pathways, but gives more information on the termination of fibres. The criteria for recognising degenerated fibres impregnated with this method are the same as those for the recognition of degeneration in suppressive Nauta stained material. Degenerated fibres however are not often seen, but when present have the same irregular, droplike appearance.

In addition to degenerating axons, and in contrast with the suppressive Nauta method, procedures I and II of Fink-Heimer impregnate numerous small spheroidal or slightly irregular structures measuring 0,5-2 micron in diameter. These are believed to be boutons terminaux for the following reasons (Fink and Heimer, 1967):

(a) such spherules are limited to regions of grey matter entered by degenerating axons;

(b) their dimensions are within the known size range of boutons terminaux, and

(c) their distribution is scattered, but sometimes indicates a localisation on the surface of perikarya, and in appropriate locations appear to outline dendritic trunks.

Electron Microscopy

Two types of terminal degeneration can be distinguished electron microscopically. These are non-filamentous (or dark) degeneration and filamentous degeneration (Westrum, 1969). They can occur either separately in specific regions (Hess, 1960; Collonier and Gray, 1962; and Westrum, 1969) or together as described by Ralston (1968).

Non-filamentous Degeneration

This type of degeneration was originally described by Hess (1960), and then in greater detail by Collonier and Gray (1962) and Westrum (1969). According to Westrum the first signs of degeneration appeared after a 24 hour survival period, and are characterised by an increased electron density and granularity of the affected boutons. After a 36 hour post-operative survival there was an increase in the number of electron opaque and granular boutons. Glycogen rich astroglial processes were also present and appeared to be engulfing dark amorphous debris in which distorted mitochondria were sometimes present. The number of degenerated boutons progressively diminished from the fifth day of survival onwards, probably due to the extreme activity

of glial cells. It is most striking to note how quickly degenerated boutons are engulfed and presumably phagocytosed by glia cells. This process seems to affect mainly the presynaptic structures (degenerating boutons). There is a relative sparing of the postsynaptic component.

Filamentous Degeneration

This type of degeneration has been described by Gray and Hamlyn (1962) in the avian optic tectum, by Glees, Meller and Eschner (1966) in the lateral geniculate body of the monkey, by Szentàgothai, Hamori and Tomböl (1966) in the lateral geniculate body of the cat, and more recently by Ralston (1969) in the ventrobasal thalamus of the cat. As is the case with non-filamentous degeneration, filamentous degeneration can occur on its own in some systems, for example the lateral geniculate body (Glees et al., 1966; Szentàgothai et al., 1966), but in others it occurs in conjunction with non-filamentous degeneration.

Filamentous degeneration is characterised by an increase in the number of neurofilaments which have the electron microscopical appearance of normal neurofilaments (Pecci-Saavedra, Vaccarezza and Mascitti, 1969). It has

been postulated that this increase in neurofibrils following damage to the neuron could constitute an unsuccessful attempt at regeneration (Gray and Guillery, 1966). The number of synaptic vescicles may appear to be reduced, probably due to swelling of the affected bouton (Ralston, 1968). The reason for the increase in neurofibrils still remains unknown. It has been shown however that this is a distinct type of degeneration, and not an intermediate stage either preceding or following non-filamentous degeneration by Ralston (1968) who followed the chronological development of both forms of degeneration in the ventrobasal thalamus.

(ii) Retrograde Degeneration

It is necessary to consider retrograde degeneration of the soma separately from that of the proximal stump (see fig. I.1), because these are demonstrated by different methods.

Retrograde degeneration of the soma has classically been demonstrated with the Nissl method which stains the endoplasmatic reticulum.

Relatively recently Grant and Aldskogius (1966) have

shown that the Nauta method is also capable of impregnating a retrograde degenerated soma. Because degeneration of the proximal stump is a process which is very similar to Wallerian degeneration it is not surprising that retrograde degeneration of the proximal stump can also be demonstrated by those methods which are normally employed for the demonstration of Wallerian degeneration. These are the Marchi method (Van Gehuchten, 1903; Mettler, 1932; and Glees et al., 1951) and the Nauta method (Cowan, Adamson and Powell, 1961; Powell and Cowan, 1964).

1. The Nissl Method

This method is capable of demonstrating changes in the soma only as it selectively stains nucleic acids and therefore demonstrates those structures like the nucleus and endoplasmatic reticulum which contain nucleic acid. The changes observed in the soma with this method, following amputation of the axon, consist of a difference in intensity of staining, the appearance of vacuoles in the cell body, an alteration in the shape and position of the nucleus, and a disappearance of the Nissl bodies from the perinuclear zone (Glees, 1961).

These changes are reversable in parts of the

central nervous system where, following the acute stage of chromatolysis the nucleus regains its central position and the Nissl substance increases to such an extent that the staining of the cells may be increased (Walker and Botterell, 1937). In the thalamus the acute stage of chromatolysis is followed by degeneration, so that a decreased number or even an absence of nerve cells was seen in Nissl stained sections (Walker, 1938).

2. The Nauta Method

The suppressive Nauta method (Nauta-Gygax, 1954) was developed as a specific method for the impregnation of anterograde degenerated fibres. According to Nauta and Whitlock (1954) and Whitlock and Nauta (1956) the Nauta method does not impregnate retrograde degenerating fibres. It has since been shown that the Nauta method is also capable of staining retrograde degenerated fibres (Cowan et al., 1961 and Powell and Cowan, 1964).

More recently Grant and Aldskogius (1966) and Grant and Westman (1968) found that the Nauta method could impregnate even cells undergoing retrograde degeneration. The underlying mechanism is however

obscure as not every soma undergoing retrograde degeneration becomes "Nauta positive". Further, these authors distinguished between two types of "Nauta positive" cells, namely those in which the impregnation was confined to the nucleus (Type I), and those in which the impregnation was confined to the cytoplasm, the nucleus remaining unaffected (Type II).

The appearance of retrograde degenerating fibres and cells, impregnated with the Nauta method, will be discussed subsequently when the problem of distinguishing between retrograde and anterograde degeneration is discussed.

3. Electron Microscopy

The appearance of neurones and dendrites undergoing retrograde degeneration is similar to that of the "dark" or "non-fibrillar" type of degenerated boutons (Grant and Westman, 1968). Retrograde degeneration of myelinated fibres has the same electron microscopical appearance as anterograde degenerated axons.

(iii) The Problem of Distinguishing Retrograde from Anterograde Degeneration

Axonal degeneration is usually studied with the Nauta method or electron microscopically. It is not possible to state whether a single degenerated axon, impregnated with the Nauta method has undergone retrograde or anterograde degeneration. It is however possible to deduce this from the general picture, as fibres undergoing anterograde degeneration are generally clumped together in thick bundles which can be traced along their complete trajectory whilst fibres undergoing retrograde degeneration are sparsely distributed and have a tendency to disappear and reappear further along their course. In electron micrographs it is not possible to state whether a single myelinated degenerated fibre has undergone retrograde or anterograde degeneration (Westrum, 1969).

Terminal degeneration can be recognised, unquestionably, with the electron microscope. Degenerated boutons can only mean terminal degeneration. Terminal degeneration can also be determined quite positively with the Glees method, in parts of the central nervous system where the boutons terminaux become hypertrophied as occurs in the lateral geniculate body of the monkey after eye enucleation. It should however be remembered that this phenomenon is very

much the exception to the rule, as these hypertrophic boutons are only found in two or three systems and in certain species. When present, it is of great diagnostic value, but otherwise the Glees method can be extremely difficult to interpret.

The criteria for distinguishing between retrograde and anterograde degeneration with the commonly used Nauta method (1957) or the Fink-Heimer modification (1967) of the original Nauta method (1950) are as follows:-

1. The duration of the survival time is extremely important as it has been shown by Powell and Cowan (1964) that anterograde degeneration definitely occurs before retrograde degeneration. By experimentally determining when retrograde degeneration starts to appear in the species used, and consequently employing a shorter survival time, one can be certain of impregnating only anterograde degeneration.

2. As retrograde fibre degeneration commences in the soma and proceeds centrifugally, the absence of retrograde degeneration as seen with the Nissl method in sections of the same material, is evidence that the degeneration seen in Nauta sections is of anterograde nature. On the other hand the concomitant presence of retrograde degeneration in Nissl sections and degenerated fibres in Nauta sections

makes the interpretation very difficult where the areas concerned are reciprocally connected.

3. Whereas the typical terminal or preterminal degeneration seen in Nauta sections has an irregular droplike appearance, retrograde changes as seen with the Nauta method appear as a diffuse, uniformly distributed granularity in all of the affected areas (Powell and Cowan, 1964).

(c) The Stereotaxic Method

To reach the central neural structures without gross damage to the overlying cerebral cortex has long been a problem in neuroanatomy, neurophysiology and neurosurgery. As a possible solution Horsley and Clark (1906, 1908) described a method by which a predetermined point in any part of the brain may be reached by a thin electrode penetrating the cortex. This method was based on the constant relationship existing between intracerebral structures and fixed cranial points. Such cranial points were difficult to establish as the skull is an irregular sphere on which most protuberances are obscured by muscles or muscle attachments (Horsley and Clark, 1908). Therefore, instead of relating the position of intracerebral structures to the surface of the skull, they proposed the

following solution:-

"We find, however, that a practicable and, on the whole, satisfactory solution of this problem may be attained by dividing the cranium into eight segments, by three section planes at rightangles to each other, e.g. sagittal, horizontal and frontal. As a result of these sections, each segment presents the three internal surfaces of a cube, and every point in it can be identified by rectilinear measurements from those surfaces or section planes, i.e. from their internal boundaries. By this means the irregular curved surface which corresponds to the three outer sides of the cube, is not involved in any way and needs no further consideration." (Horsley and Clark, 1908).

As constant cranial reference points the orbit and external auditory meatus were used. The horizontal baseline of Horsley and Clark (1908) runs from the middle of the lower orbital margin to the middle of the external auditory meatus. The frontal section plane is perpendicular to the horizontal or basal plane and passes through the centres of both external auditory meati. The sagittal section plane is perpendicular to the previous two planes and is situated mid-sagittally.

From a stereotaxic atlas the horizontal, frontal and sagittal co-ordinates of a particular intracerebral structure can be obtained. The atlases used in this study were those of Ingram, Hannet and Ranson (1932), Jasper and Ajmone-Marsan (1954), Snider and Niemer (1961) and Reinoso-Suàrez (1961). The experimental animal is placed in the stereotaxic apparatus which is set to the co-ordinates of the nucleus in question. The tip of the electrode will then reach this nucleus, depending on the accuracy of the atlas, and the degree of individual variation within the species used.

CHAPTER II

THE CYTOARCHITECTURE OF THE PULVINAR

A subdivision of the primate pulvinar into four parts is generally accepted, and is adhered to throughout this work. The description which follows of the topography and cytoarchitecture of these four subdivisions is based on the work of Ingram, Hannet and Ranson (1932), Jasper and Ajmone-Marsan (1954), Snider and Niemer (1961) and Reinoso-Suàrez (1961) in the case of the cat. Photomicrographs and drawings obtained in the course of the present investigation have been used to illustrate the features of this classification. The subdivisions of the primate pulvinar are described using three coronal, Nissl stained sections through the pulvinar of the Macaca mulatta.

Nucleus Pulvinaris Oralis

In coronal sections this nucleus appears between n. centrum medianum and n. ventralis posterior lateralis of the thalamus. Its caudal border is approximately at the caudal tip of n. ventralis posterior lateralis (fig. II.1). The cell density in general is less than in the other subdivisions of the pulvinar, and this area is not traversed by any large fibre bundles.

Nucleus Pulvinaris Lateralis

This nucleus lies between the n. pulvinaris medialis medially, the n. pulvinaris inferior inferiorly, and is bordered supero-laterally by the lamella medullaris externa. It is composed of small lightly-stained cells arranged in bands which give the nucleus a typical striped appearance. Between these bands of cells long fibre bundles are present which extend from the lamella medullaris externa medially and medioventrally (figs. II.2 and II.3).

Nucleus Pulvinaris Medialis

At its rostral end this nucleus appears between n. mediodorsalis medially and n. pulvinaris lateralis laterally. The lateral ventricle and fornix lie superiorly and the n. limitans and pulvinar oralis inferiorly (fig. II.1). More caudally its lateral relation remains the n. pulvinaris lateralis while inferiorly it is related to n. pulvinaris inferior and inferomedially to the brachium colliculus superior (fig. II.2). Medially its caudal part borders on the third ventricle, superomedially it is related to the fornix and superiorly to the lateral ventricle. It is composed of evenly dispersed, medium-sized cells. Unlike the n. pulvinaris lateralis it is free of fibre bundles except in its ventro-medial border (fig. II.2). These bundles originate from the brachium colliculi superioris.

Nucleus Pulvinaris Inferior

This nucleus appears ventral to the lateral geniculate body and lateral to the medial geniculate body (fig. II.2). More caudally it is separated from the rest of the pulvinar by the brachium colliculi superioris. It is very cellular and characterised by the presence of large and darker-stained cells among the more typical medium-sized cells.

The pulvinar of the cat is shown in figures II.4 and II.5 which are photomicrographs of coronal Nissl stained sections through the oral and caudal parts of the pulvinar. In the cat the pulvinar is a poorly differentiated region in the dorsolateral corner of the caudal part of the thalamus. Superiorly it is related to the lateral ventricle, supramedially to n. lateralis dorsalis, inferomedially to n. lateralis posterior and inferolaterally to the lateral geniculate body. The exact boundaries between n. lateralis dorsalis and pulvinar are difficult to define. The cells are medium-sized and lightly stained and, especially in its more lateral part, also arranged in "stripes" or "bands". This is the result of fibres from the thalamic radiation which enter or leave the pulvinar from its superolateral aspect. It will be clear on comparing figures II.1, II.2 and II.3 with figures II.4 and II.5 that a subdivision of the pulvinar on cytoarchitectural grounds, as it is possible in the Simian, is impossible in the cat.

ABBREVIATIONS

Ann	-	Nucleus annularis
BCI	-	Brachium colliculi inferioris
BCS	-	Brachium colliculi superioris
BP	-	Brachium pontis
CC	-	Corpus callosum
Cd	-	Nucleus caudatus
CM	-	Nucleus centrum medianum
CS	-	Colliculus superior
DBC	-	Decussatio brachii conjunctivi
Dt	-	Nucleus of Darkschewitsch
F	-	Fornix
FLM	-	Fasciculus longitudinalis medialis
FRP	-	Formatio reticularis pontis
FRTM	-	Formatio reticularis tegmenti mesencephali
GC	-	Griseum centrale
GP	-	Griseum pontis
HL	-	Habenula lateralis
HM	-	Habenula medialis
IP	-	Nucleus interpeduncularis
LG	-	Corpus geniculatum laterale
LGv	-	Corpus geniculatum laterale pars ventralis
Li	-	Nucleus limitans
Lld	-	Nucleus lemnisci lateralis, pars dorsalis
Llv	-	Nucleus lemnisci lateralis, pars ventralis
LML	-	Lemniscus lateralis
LP	-	Nucleus lateralis posterior
MD	-	Nucleus medialis dorsalis
MG	-	Corpus geniculatum mediale
mc	-	Corpus geniculatum mediale, pars magnocellularis
MIN	-	Nucleus medialis interlaminaris
N III	-	Nucleus III
N IV	-	Nucleus IV
NRT	-	Nucleus reticularis thalami
P	-	Nucleus pulvinaris
PC	-	Commisura posterior
PI	-	Nucleus pulvinaris inferior
PL	-	Nucleus pulvinaris lateralis
PM	-	Nucleus pulvinaris medialis
PO	-	Nucleus pulvinaris oralis
Po	-	Nucleus posterior
PT	-	Regio praetectalis
Pg	-	Nucleus praegeniculatus
THP	-	Tractus habenulo-interpeduncularis
TO	-	Tractus opticus
SG	-	Nucleus supragenicularis
V	-	Nervus V

Fig. II. 1.

Fig. II. 2.

Fig. II. 3.

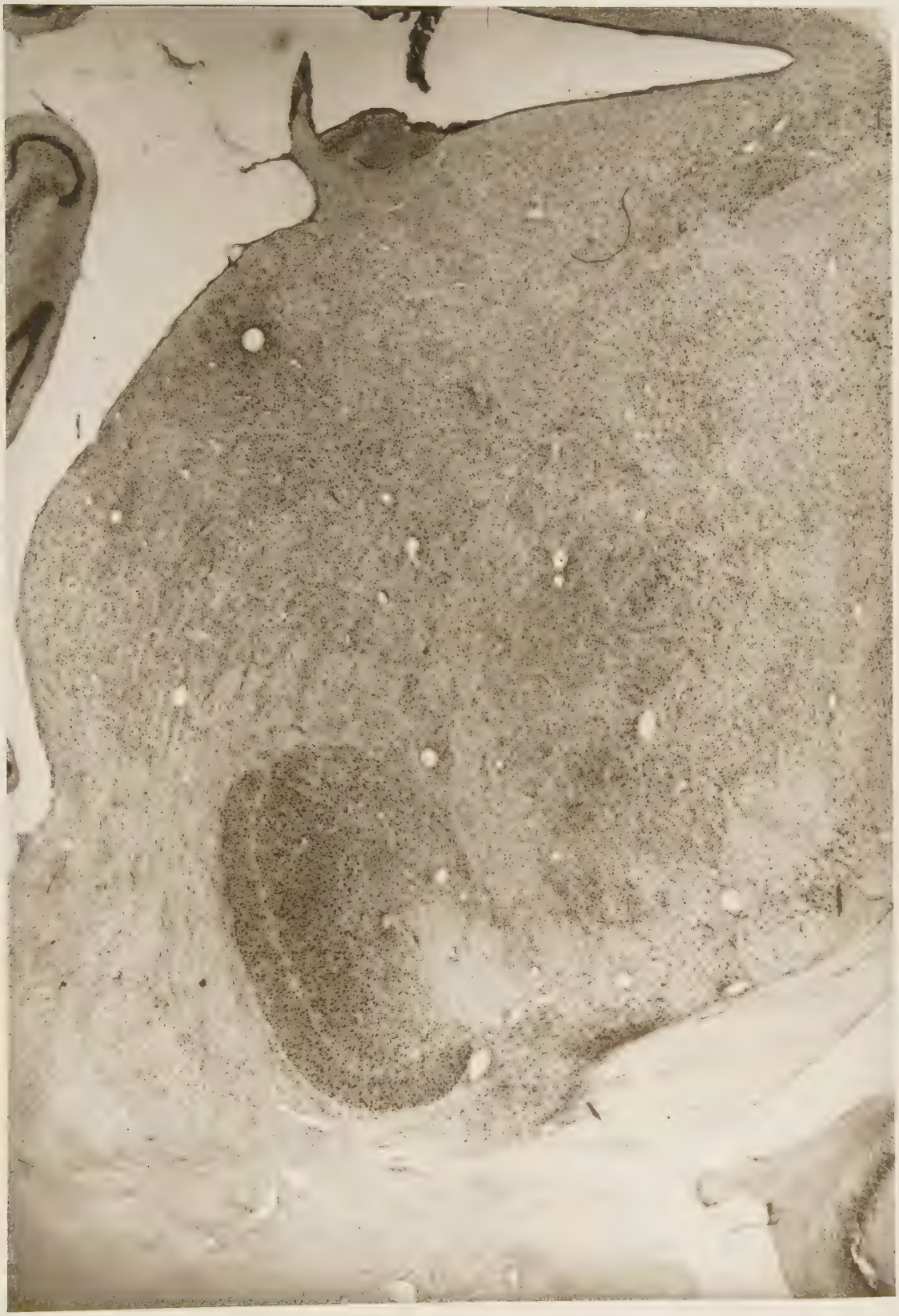


Fig. II. 4.

Fig. II. 5.

CHAPTER III

THE RETINO-PULVINAR PROJECTION

III.1 GENERAL

As was pointed out in the introduction, a great deal of controversy exists about this projection. Thus Minkowski (1921) found evidence of a retino-pulvinar projection in the rabbit and goat, but none in the Macaca mulatta and man. On the other hand, Hassler and Wagner (1965) described two cases of human anophthalmia with striking atrophy of the inferior pulvinar.

There are quite considerable differences between the retinal projection of the cat and the primate. In addition to the lateral geniculate body the cat has two other nuclei possibly concerned with the visual system. Firstly there is the medial intralaminar nucleus (MIN) which has a retinal projection forming a "mirror image" of the retinal projection onto the lateral geniculate body (Heyhow, 1958). Secondly there is the nucleus posterior of Ingram, Hannet and Ranson (1932) which, according to neurophysiological evidence (Kingston, Vadas and Bishop, 1969) receives a retinal projection. This projection has not been demonstrated neuroanatomically (Heyhow, 1958).

With these difficulties in mind we selected particular animals for this part of our investigation.

To represent the subprimates we chose the Göttingen dwarf pig, as the visual system of this animal has not yet been investigated, while the visual system of the cat has been extensively studied by other workers (Heyhow, 1958; Laties and Sprague, 1966; Stone and Hansen, 1966; Garey and Powell, 1968). Because we employed the same methods as these authors, we did not attempt to repeat their investigation.

To represent the primates we chose a member of the suborder Prosimii, the Galago crassicaudatus, and three members of the suborder Simii, Cebus cappuccinus, Macaca mulatta and Papio ursinus. We concentrated upon the Galago crassicaudatus and Papio ursinus while only two animals of each of the other species were used, to attempt to corroborate our findings.

It is clear that there exists a rather large gap, from a phylogenetic point of view, between the pig and the bushbaby. Furthermore these animals do not form "a graded evolutionary series" (Le Gros Clark, 1930). This makes it very difficult to establish whether the pig or cat pulvinar is a true homologue of the primate pulvinar. This was not however the purpose of our study. We are by no means attempting to bridge the gap between cat and primate, but rather attempting to establish whether our knowledge of the cat (or pig) pulvinar

is at all applicable to the primate pulvinar.

III.2 MATERIAL AND METHODS

(a) The Pig

The Göttingen dwarf pig, a cross between the domestic pig, Sus scrofa, and the dwarf pig, Sus vitatus was used for this investigation. Seven pigs were used. The bodyweights ranged from 28 Kg. to 34 Kg.

(i) Anaesthesia

The pigs were found to be very resistant to ether and Fluothane and were therefore induced with intravenous Nembutal. Anaesthesia was maintained with ether given by the open drip method. The pigs were not intubated or artificially ventilated in any way.

(ii) Operation

A unilateral eye-enucleation was performed in six pigs, and the seventh was used as a control animal. The enucleation was done as follows. The eyelids were retracted and the inferior conjunctival fold incised. The globe was then drawn slightly forward. The optic nerve and vessels were tied off and amputated at their point of entry to the globe. Chloromycetin ointment was

placed in the cavity, and the eyelids were then loosely sutured together.

(iii) Perfusion

After a post-operative survival period of 6 to 20 days, the animals were perfused under Nembutal anaesthesia. This was done by opening the abdominal cavity to expose the aorta. As large a rubber catheter as possible was introduced into the aorta and advanced as far as the aortic arch. The chest was then opened and the right ventricle incised. The brain was perfused with a 10% formol-saline solution for 15 to 20 minutes and then removed and post-fixed in 10% formol-saline for six weeks.

(iv) Sectioning and Staining

To facilitate the sectioning each brain was cut into three blocks. Most of the cortex was cut away as it was of no interest in this part of the investigation and considerably complicated the mounting of the sections. Serial frozen sections were then made of the remaining brain. From each brain four comparable series were obtained. Three of these consisted of sections 25 microns thick while the fourth consisted of sections 50 microns thick. The first three series were stained by

the methods of Glees (1946), Nauta and Gygax (1954), and Procedure II of Fink and Heimer (1967) respectively, while the 50 microns thick sections were stained with cresylviolet as a topographical control.

As is usual in this type of study, the cresylviolet sections were projected and trace drawings made. On the drawings obtained in this way the patterns of degeneration observed in the Glees, Nauta, and Fink-Heimer sections were filled in.

(b) Galago crassicaudatus

Seventeen normal adult animals of this species were used. Their body weights ranged from 400 to 600 grams.

(i) Anaesthesia

From previous experience (Campos-Ortega and Cluver, 1968) we knew the Galago to be very excitable, with the result that it takes very long to respond to intraperitoneal Nembutal. Further there appears to be a small margin between the minimum effective dose and lethal dose when the animals are in a very anxious state. In order to obtain a short induction period, as well as a good degree of control over the depth of anaesthesia,

Fluothane was used both for induction and maintenance of the anaesthesia. This was administered by the open drip method.

(ii) Operation

Of the 17 Galago, 2 were used as control animals; in 8 a unilateral eye enucleation was performed; and in 7 a localised retinal coagulation. The procedure for the eye enucleation was identical to that described above in the pig. The retinal coagulation was made with a Zeiss photocoagulator after atropinizing the eye. In three of these cases a macular lesion was made and in the remaining four a different retinal quadrant was coagulated in each case.

(iii) Perfusion

After a post-operative survival period ranging from 4 to 20 days the animals were perfused in the same way as described for the pig.

(iv) Sectioning and Staining

Serial sections were made of the complete brain as it is small and the frozen sections easier to mount than in the case of the pig or baboon. Otherwise the methods used for sectioning and

staining were the same as those used in the case of the pig.

(c) Cebus cappucinus

Three normal adult monkeys of this species were used. Their body weights ranged from 2.5 to 3.5 Kg.

(i) Anaesthesia

Fluothane anaesthesia, as described above for the Galago, was used for the same reasons.

(ii) Operation

Two animals were used as controls while on the third an eye enucleation was performed using the same technique as described for the pig.

(iii) Perfusion

After a ten-day post-operative survival period the subject animal was perfused, as were the controls, under intraperitoneal Nembutal anaesthesia, as described above for the pig.

(iv) Sectioning and Staining

Complete series of frozen sections were made of all three brains. The same methods of

sectioning and staining were used as described in the case of the pig.

(d) Macaca mulatta

Three normal adult monkeys of this species were used. Their body weights ranged from 5.5 to 6.5 Kg.

(i) Anaesthesia

The Macaca was found to respond quite well to intravenous Valium. This resulted in a stuporose state in which the monkeys were easily manageable. Complete anaesthesia for the operative procedure was obtained with Fluothane.

(ii) Operation

A unilateral eye enucleation was performed in one monkey, and the other two kept as controls. The operative procedure was the same as described in the case of the pig.

(iii) Perfusion

After a survival period of 10 days the subject animal was perfused as were the controls, under Nembutal anaesthesia, as described above for the pig.

(iv) Sectioning and Staining

These brains also were sectioned and stained in the same way as described for the pig.

(e) Papio ursinus

Ten normal adult baboons of this species were used. Their body weights ranged from 9 Kg. to 11.5 Kg. Unlike the previous cases, which were all operated on in the Institut für Experimentelle Neuroanatomie in Göttingen, West Germany, the baboons were operated on in the primate centre of the University of Stellenbosch at Karl Bremer Hospital.

(i) Anaesthesia

The baboons were given Syrnalon (Then-Cyclidene HCl) by intramuscular injection using a squash cage. This drug induced a passive, semi-stuporose state, in which the baboon could be easily handled. Thereafter the baboons were given intravenous Valium which, in addition to producing a deeper state of anaesthesia, also inhibited the muscular twitchings caused by the Syrnalon. The baboons were intubated and the desired level of anaesthesia maintained with a mixture of nitrous oxide and oxygen given with a Boyles machine.

(ii) Operation

In three baboons (Pa 1, Pa 2, and Pa 3) a unilateral eye enucleation was performed, using the same technique as previously described for the pig. In four baboons (Pa 4, Pa 5, Pa 6, Pa 7) a localised retinal electro-coagulation was performed. The remaining three (Pa 8, Pa 9, and Pa 10) were used as normal control animals. The retinal coagulations were performed as follows. The eyelids were retracted and the inferior conjunctiva incised to free the globe. It was attempted to coagulate one quadrant of the retina in each case. The position of the macula and the four quadrants was determined from the point of entrance of the optic nerve. The coagulation was performed with a blunt electrode resting on the sclera. The position and size of the coagulation was observed immediately afterwards with an opthalmoscope.

(iii) Perfusion

This was performed under Syrnalon and Valium anaesthesia after a survival period of seven to ten days. The technique was that described previously for the pig.

(iv) Sectioning and Staining

The brains were sectioned and stained in the

same way as has been described for the pig.

III.3 RESULTS

(a) The Göttingen Dwarf Pig

The distribution and termination of the retinal fibres were observed light microscopically in Glees (1946), Nauta and Gygax (1954) and Fink and Heimer (1967) stained sections. The findings in the six pigs used in the investigation were identical.

The proportion of crossed and uncrossed retinal fibres was found to be approximately 9:1.

The fibres terminated, rostrocaudally, in the ventral lateral geniculate body (L.G.B.v), then in the dorsal lateral geniculate body (L.G.B.d), and then in the more medially situated medial interlaminar nucleus (M.I.N.) (fig. III.1 A-F).

Caudal to the L.G.B.d and M.I.N. the degenerated retinal fibres could be seen following two different courses (fig. III.1 C and D). The more dorsal of these ran along the stratum zonale thalami, while the ventral traversed the thalamus including part of the pulvinar. All these fibres terminated rostrocaudally, in the pre-

tectal region in the nucleus limitans (Li) and in the more medially situated nucleus tractus opticus (N.t.o.) (fig.III.1 C). The fibres traversing the pulvinar were degenerated, but this was purely degeneration "en passage", with no signs of terminal degeneration. (Where a fibre tract appears to be degenerated at a point along its course without signs of boutonal degeneration, this is commonly referred to as degeneration "en passage".) The degeneration "en passage" is shown in figureIII.1 B, C and D.

Further caudally the fibres terminated in the stratum zonale, griseum superficiale and stratum opticum of the superior colliculus.

In normal material it is difficult to recognise the presence of lamination in the pig's L.G.B.d. After eye enucleation it became obvious, in Nauta stained sections, that the optic fibres were distributed to three different laminae. The more lateral and the more medial of these were related to the contralateral retina, while the middle lamina was related to the ipsilateral retina.

Between laminae 1 and 2 there were a group of longitudinally orientated cells, which appear to correspond with the cells found in the interlaminar

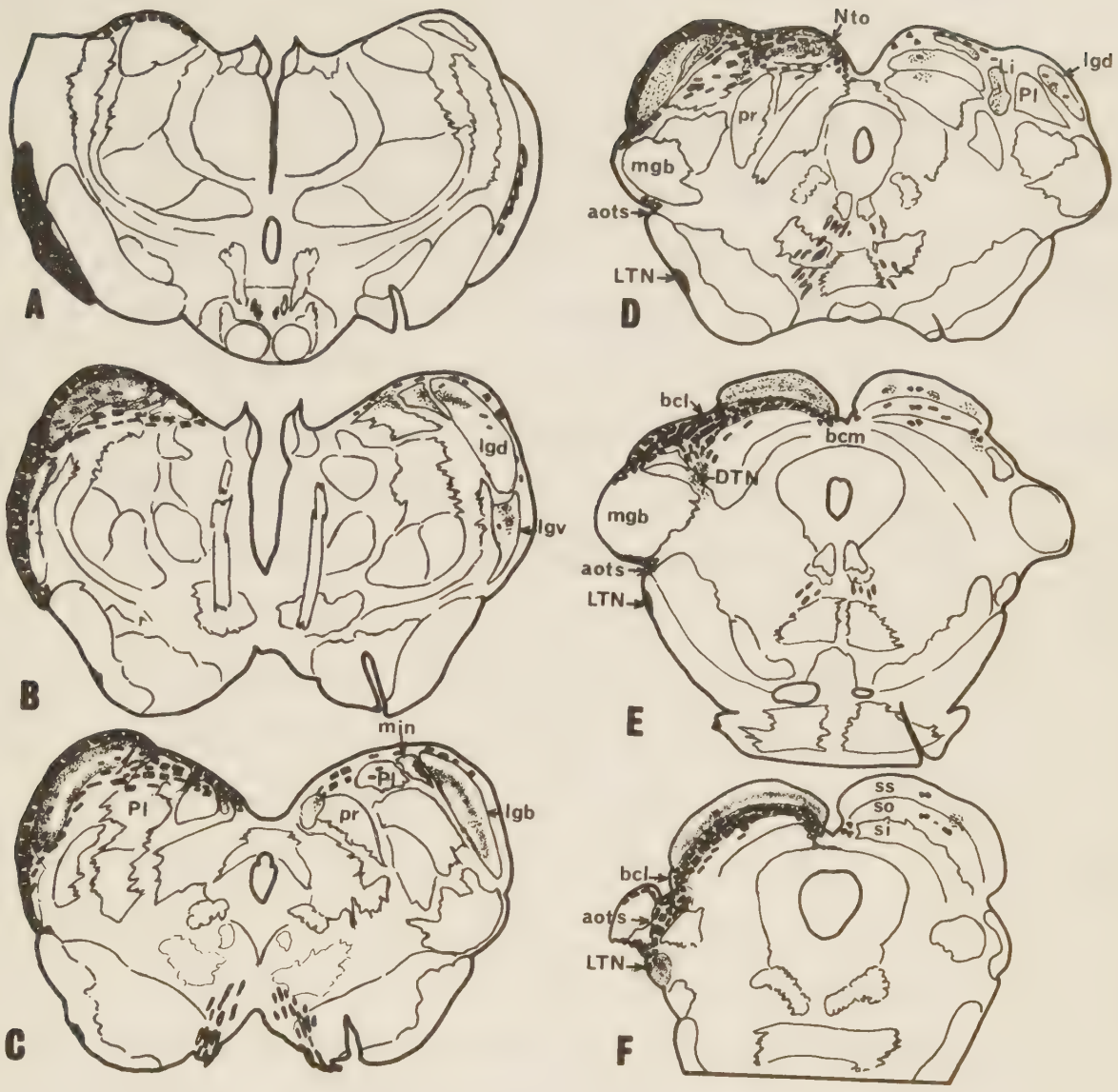


Fig. III.1

The diagram shows the distribution of degenerated retinal fibres in the pig. Fine dots represent terminal degeneration and large dots degeneration "en passage".

Abbreviations: aots: Accessory optic tract; bcl: brachium colliculi superioris (lat); bcm: brachium colliculi superioris (med); DTN: Dorsal terminal nucleus; LTN: lateral terminal nucleus; lgd: dorsal lateral geniculate body; lgv: ventral lateral geniculate body; Li: Nucleus limitans; Nto: nucleus tractus opticus accessorius; Pl: pulvinar; pr: nucleus praetectalis; Si: Stratum griseum intermedius; SO: stratum opticum; ss: stratum griseum superficiale; mgb: medial geniculate body; min: medial interlaminar nucleus.

fibre plexus A-A1 of the cat. These cells are pointed out by two arrowheads in fig.III.2 A. Terminal degeneration was seen in layer 2 as well as in the interlaminar fibre plexus between layers 1 and 2 of the ipsilateral L.G.B.d. In the contralateral L.G.B.d the fibres terminated in layers 1 and 3. Ipsilateral termination of retinal fibres in the L.G.B.d is shown in figureIII.2 C, in which the interlaminar fibre plexus is delimited by four arrowheads. The L.G.B.d of the pig therefore has a trilaminar organisation with fibres of the ipsilateral retina terminating in layer 2 and fibres from the contralateral retina terminating in layers 1 and 3.

Medial to the L.G.B.d there was a small triangular nucleus, the medial intralaminar nucleus (M.I.N.), which is delimited by three arrows in figureIII.2 A. The M.I.N. was an independent nucleus separated from the pulvinar and the L.G.B.d by a thin fibrillar capsule. In Nissl stained sections it had a uniform appearance, but in Nauta stained sections, of cases with a unilateral eye enucleation, a concealed lamination became apparent. Like the L.G.B.d it had a trilaminar organisation and a bilateral retinal innervation. The ipsilateral retinal fibres terminated in the middle part, while the contralateral fibres terminated in the dorsal and ventral parts.

Figure IV.2 B shows the termination of ipsilateral fibres in the ipsilateral nucleus. The M.I.N. therefore appears to be a mirror image of the L.G.B.d.

(b) Galago crassicaudatus

The distribution and termination of retinal fibres were observed light microscopically in the Glees (1946), Nauta Gygax (1954) and Fink-Heimer (1967) stained sections. The findings in the 8 animals in which unilateral eye enucleations were performed were identical.

The proportion of crossed to uncrossed retinal fibres was found to be approximately 1:1.

The first relay station of the retinal fibres was the pregeniculate nucleus which lay rostromedially to the lateral geniculate body. Degenerated fibres terminated in its ventrolateral part. Caudal to this, degenerated fibres terminated in alternate layers of the L.G.B. which had a typical primate appearance.

The fibres to the pretectal region followed two different courses: the more rostral fibres ran along the stratum zonale of the pulvinar, while the more caudal fibres traversed the inferior pulvinar. Both fibre bundles showed only degeneration "en passage". Terminal degeneration was seen in the pretectal region

Fig. III.2 A

This shows a cresyl violet stained coronal section of the lateral geniculate body of the pig. The three arrows delimit the medial interlaminar nucleus. The two arrowheads point to the interlaminar fibre plexus.

Fig. III.2 B

This shows a Nauta stained coronal section of part of the lateral geniculate body. Degenerated fibres are present in the central part of the picture.

Fig. III.2 C

This shows a Nauta stained section of part of the lateral geniculate body. The arrowheads delimit the interlaminar fibre plexus containing degenerated fibres

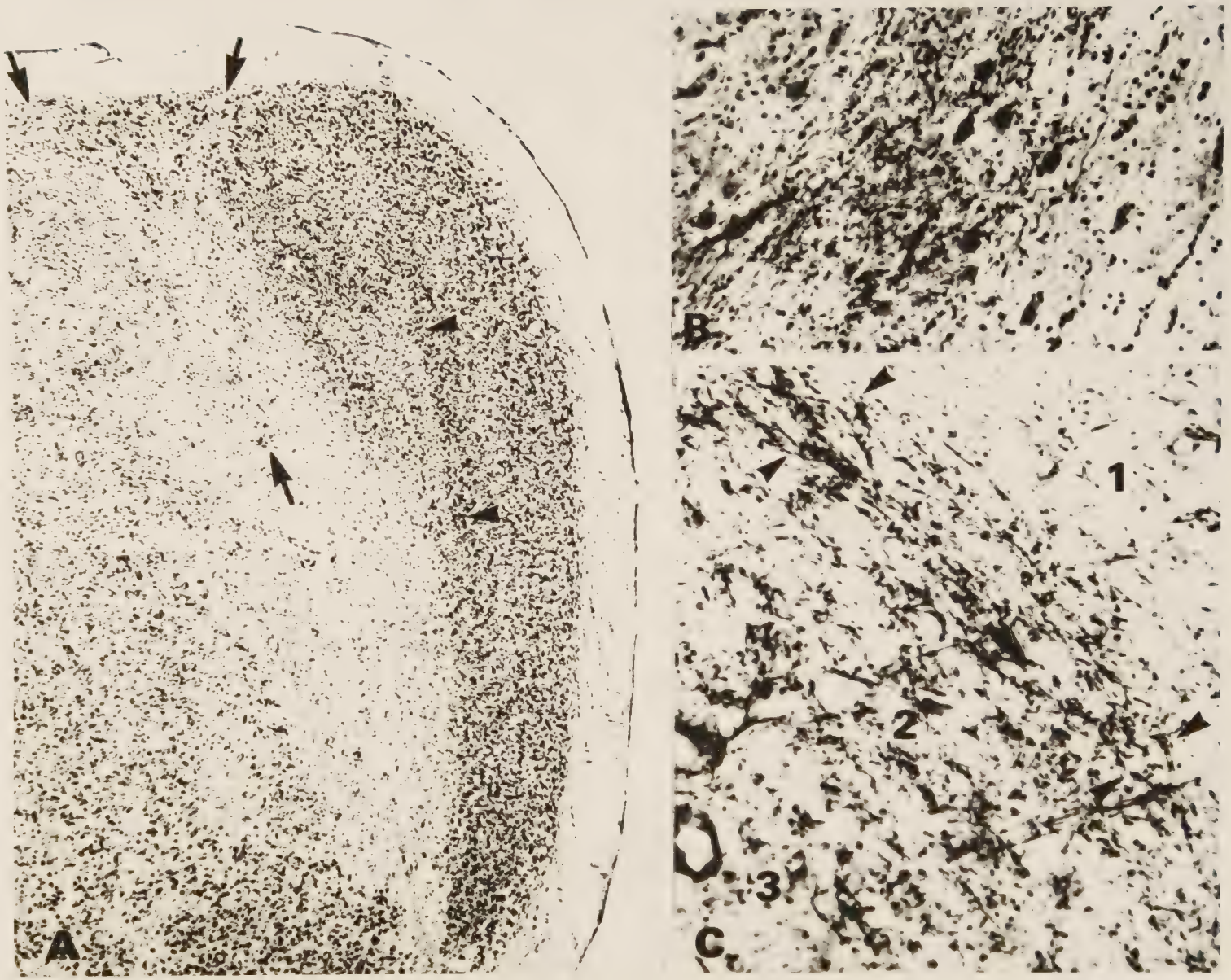


Fig.III.3

The diagram shows the distribution of the degenerated retinal fibres after unilateral eye enucleation. Five selected sections were drawn with the help of a projector. On the left side of each section the contralateral degenerated fibres are presented. The fine dots represent terminal degeneration and the large the pre-terminal and degeneration "en passage".

Abbreviations: A: centrum medianum; BCSl: brachium colliculi superioris pars lateralis; BCSm: brachium colliculi superioris pars medialis; bi: brachium colliculi inferioris; cgl: corpus geniculatum laterale; cgm: corpus geniculatum mediale; li: n. limitans; lvp: n. lateralis ventralis posterior; OAc: n. tractus opticus accessorius; pg: n. praegeniculatus; pi: n. pulvinaris inferior; pm: n. praetectalis medialis; pt: n. praetectalis; pul: pulvinar; rt: n. reticularis thalami; so: stratum opticum; sp: n. supragenicularis; ss: stratum griseum superficiale; sz: stratum zonale thalami; toa: tractus opticus accessorius.

in the nucleus limitans and medial pretectal nucleus. There were no signs of terminal degeneration in the stratum zonale or inferior division of the pulvinar.

The fibres to the tectum consisted mainly of crossed fibres which, as was the case with the retino-pretectal fibres, followed two courses. Fibres of the lateral course, or brachium colliculi superioris pars lateralis, left the caudal aspect of the optic tract and passed around the medial geniculate body and caudal part of the pulvinar to terminate in the stratum zonale, griseum superficiale and opticum of the superior colliculus. The medial course, or brachium colliculi superioris pars medialis, lay caudal to the caudal pretectal fibres which traverse the inferior pulvinar. The fibres following this medial course eventually terminated in the regio praetectalis and stratum opticum of the superior colliculus. Although both fibre components to the tectum were in contact with the pulvinar at some point along their path, there were no signs of terminal degeneration until they reached the superior colliculus.

(c) Cebus cappucinus and

(d) Macaca mulatta

The results in these two monkeys were found to be so similar to those obtained in the baboon, that they will not be described separately. The minor differences

which do exist will be described with the results obtained from the baboons.

(e) Papio ursinus

The distribution and termination of retinal fibres were observed light microscopically in Glees (1946), Nauta Gygax (1954) and Fink Heimer (1967) stained sections. The findings in baboons Pa 1, Pa 2 and Pa 3 in which unilateral eye enucleations were performed were identical. The findings in baboons Pa 4, Pa 5, Pa 6 and Pa 7 in which local retinal coagulations were performed were similar. Unfortunately none of the retinal coagulations were found to be restricted to a single quadrant as was intended. Case Pa 6, with the most localised lesion of the four, will be described.

The proportion of crossed to uncrossed retinal fibres was found to be approximately 1:1.

The distribution of retinal fibres was similar to that found in Galago. Rostrocaudally the fibres terminated first of all in the pregeniculate nucleus (fig.IV.7 A and B).

Caudal to this a large number of fibres terminated in the lateral geniculate body. The lateral geniculate

body had the typical primate appearance consisting of two macrocellular layers inferior to a number of medium and small celled layers. Altogether the baboon LGB had eight layers. The retinal fibres terminated in alternate layers (fig. III.4).

Immediately medial to the LGB there was a narrow band of cells with similar appearances to those of the LGB. These cells are pointed out by arrowheads in figure III.5. They are known as the intermediate cell group of Minkowski (1920). Figure III.4 shows 12 consecutive coronal sections through the contralateral LGB and inferior pulvinar of case Pa 1. The areas containing degenerated boutons are shown in solid black. As is shown in figure III.4, degenerated boutons were seen in the intermediate cell group of Minkowski in sections 17, 18, 20 and 21. In sections of the ipsilateral LGB of case Pa 1 degenerated boutons were also seen in the intermediate cell group of Minkowski (fig. III.6, sections 11-16). Degeneration in both the right and left intermediate cell groups of Minkowski was also observed in the other cases Pa 2 and Pa 3.

In case Pa 6 a unilateral retinal coagulation was performed affecting the inferior temporal macula, the inferior temporal peripheral quadrant and a small part of the inferior nasal peripheral quadrant. The

Fig. III.4

The diagram shows consecutive sections of the lateral geniculate body and inferior pulvinar of the baboon following contralateral eye enucleation.

The lateral geniculate body can be seen to consist of 8 layers in which the retinal fibres terminate in alternate layers. The layers in which degenerated boutons were seen are shown in solid black. The inferior pulvinar is first seen in section 24. Groups of degenerated boutons are shown in solid black in the inferior and lateral parts of the inferior pulvinar.

In sections 17 to 21 degenerated boutons were present in the intermediate cell group of Minkowski.

Fig. III.4 The diagram shows consecutive sections of the lateral geniculate body and inferior pulvinar of the baboon.

Fig. III. 5. A cresylviolet stained section of the lateral geniculate body of the baboon.

resulting pattern of degeneration in both the ipsi- and contralateral LGB is shown in figure III.9. The intermediate cell group of Minkowski was completely free from degenerated boutons on both sides.

In case Pa 1, small islands of degenerated boutons were seen along the inferior and lateral border of the inferior pulvinar. These degenerated boutons were present both on the contralateral side (fig. III.4, sections 24-28) as well as on the ipsilateral side (fig. III.6, sections 15-18). Similar findings were obtained in case Pa 2. Case Pa 3 was sectioned sagittally and, as far as degeneration in the inferior pulvinar is concerned, was more informative than the other two. In sagittal, Nissl stained sections of the inferior pulvinar, small islands of cells could be seen along its inferior and lateral border. These cells were larger and darker stained than the rest of the cells of the inferior pulvinar (fig. III.8). The degenerating boutons of optic fibres were seen in the immediate vicinity of these cells in Glees and Nauta stained sections of case Pa 3 (fig. III.7, A and B).

The retinal fibres to the pretectal and tectal regions followed a course similar to that described for the Galago, and terminated in the same nuclei.

Fig. III.6

The diagram shows consecutive sections of the lateral geniculate body and inferior pulvinar of the baboon following ipsilateral eye enucleation.

The lateral geniculate body can be seen to consist of 8 layers in which the retinal fibres terminate in alternate layers. The layers in which degenerated boutons were seen are shown in solid black. The inferior pulvinar is first seen in section 24. Groups of degenerated boutons are shown in solid black in the inferior and lateral parts of the inferior pulvinar.

In sections 11 to 16 degenerated boutons were present in the intermediate cell group of Minkowski.

Fig. III.6 The diagram shows consecutive sections of the lateral geniculate body and inferior pulvinar of the baboon.

Fig. III.7

The diagram shows two sagittal sections of the pulvinar and adjacent structures of the baboon.

Groups of degenerated boutons, shown as large dots, are pointed to in the inferior pulvinar by arrowheads. Degenerated boutons were seen in the pregeniculate nucleus where they are shown as small dots. Between the pulvinar and the pregeniculate nucleus lies the lateral geniculate body, where layers containing degenerated boutons are shown in solid black. The configuration of layers is not as clear as is the case in coronal sections.

Fig. III.7 Sagittal sections of the pulvinar and adjacent structures.

Abbreviations: PL: lateral pulvinar; PI: inferior pulvinar; PG: praegeniculate nucleus; RT: reticular nucleus of thalamus.

The findings in Cebus and Macaca were very similar to those for Papio with the following exceptions. The intermediate cell group of Minkowski were less pronounced in Cebus and Macaca and the number of degenerated retinal boutons in the inferior pulvinar were less. Although not conclusive evidence,as only one experimental animal of each of these species was used, the impression was gained that the number of degenerated retinal boutons present in the inferior pulvinar progressively increased from Cebus to Macaca to Papio.

III.4 DISCUSSION

The purpose of the experiments was to determine the extent of the retinal projection in various species. Special attention was given to the pulvinar, in an attempt to establish its role in the primary visual system.

The results have shown that the primary visual system of the pig closely resembles that of the cat, but differs considerably from that of any of the simians investigated. This difference appears so great that it seems impossible to establish any homologies between subprimate and simian visual systems at first. Could this discrepancy be due to nuclei like the feline M.I.N. becoming incorporated in the simian pulvinar or L.G.B. ? Before we attempt to determine this, each of the relevant nuclei will be discussed.

In the lower mammals two lateral geniculate bodies are recognised, namely a dorsal and a ventral one. The dorsal lateral geniculate body develops rapidly in phylogeny, to become a large laminated nucleus in the primate, while the ventral lateral geniculate body undergoes a relative regression and becomes the comparatively small pregeniculate nucleus of the primate. Because of rotation occurring during the process of development, the relative positions of the two nuclei are reversed in comparison with the original phylogenetical condition, the larger laminated nucleus assuming a ventral, and the pregeniculate nucleus a dorsal position in the primate (Polyak, 1955).

The retina projects directly to the pretectum and tectum in the pig and the primates studied by us. Our impression that this projection is relatively larger in the lower animals, when compared with the retino-geniculate projection, confirms the opinion of Polyak (1955).

The major primary visual centres have presented no problems from a comparative anatomical point of view. Establishing a homologue really becomes a problem with the smaller primary visual nuclei like the M.I.N. and nucleus posterior.

The medial intralaminar nucleus (M.I.N.) was first

described by Heyhow (1958) in the cat. He originally thought that this nucleus was a pure feline characteristic, but this view was proved incorrect when he found a M.I.N. in the marsupial phalanger (Heyhow, 1967). Shortly afterwards he was also able to demonstrate this nucleus in the sheep (Heyhow, 1969). We have now been able to demonstrate the presence of a M.I.N. in the pig. This nucleus is medial to the L.G.B.d and receives retinal fibres in such a way that it forms a mirror image of the L.G.B.d. It therefore receives a point to point projection from the whole retina similar to the L.G.B.d. Concealed lamination of the M.I.N. becomes apparent after eye enucleation. This nucleus is not found in primates, but it may have been incorporated into the L.G.B. as the intermediate cell group of Minkowski or into the pulvinar.

The nucleus posterior was first described by Ingram, Hannet and Ranson (1932) in the cat. It is a wedge shaped mass of cells lying in the angle between the two geniculate bodies. This area was considered part of the pulvinar by Pines (1927). We were able to recognise a similar collection of cells in the pig, but found no evidence of a retinal projection to this area. This coincides with the findings of a number of authors on the cat (Heyhow, 1958; Laties and Sprague, 1969; Stone and Hansen, 1966; and Garey and Powell, 1968). There is however strong neurophysiological evidence

Fig. III.8

This shows a photomicrograph of a cresylviolet stained sagittal section of the pulvinar and lateral geniculate body of the baboon.

It shows the same area as the diagrams in figure III.7 on page 89.

Arrowheads point to large, dark staining, cell clusters along the inferior and lateral borders of the inferior pulvinar. These can be seen to occupy a similar position to the degenerated boutons in the inferior pulvinar shown in figure III.7.

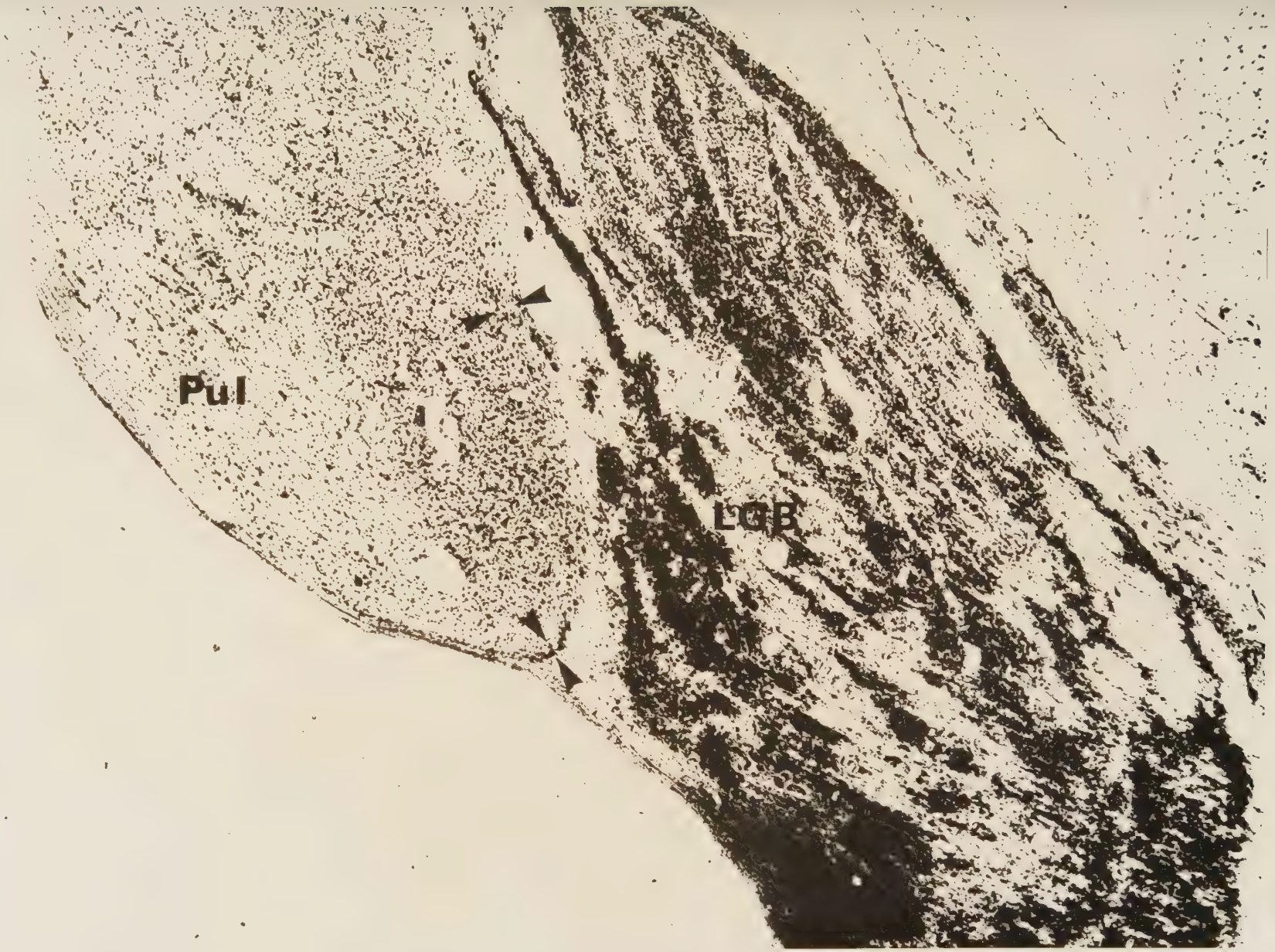


Fig. III. 8. A sagittal section of the pulvinar and lateral geniculate body of the baboon.
Abreviations : Pul: lateral pulvinar; Pui: inferior pulvinar; L.G.B.: lateral geniculate body.

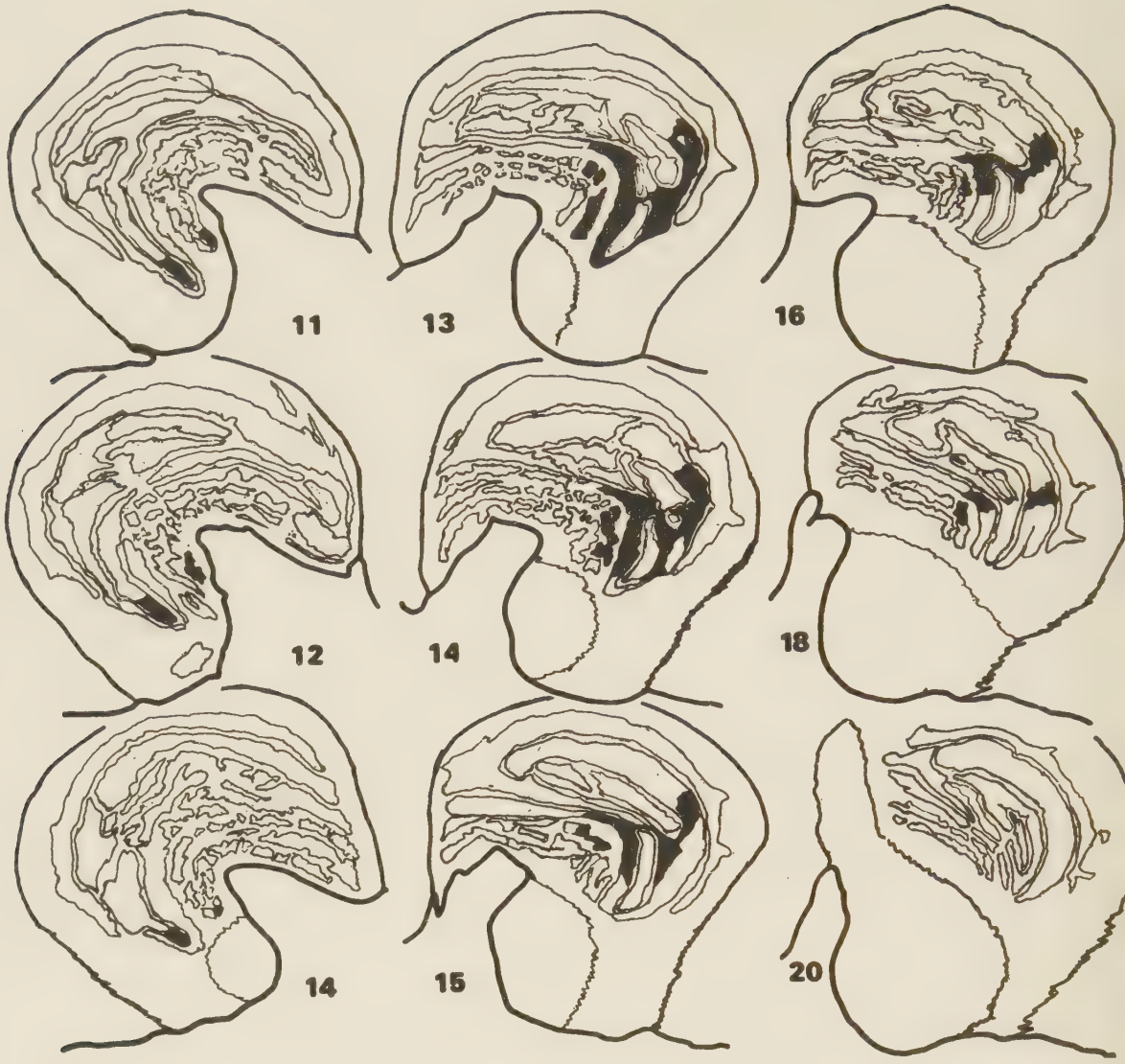


Fig. III.9

The diagram shows coronal sections of both lateral geniculate bodies of baboon Pa 6. Sections 11, 12 and 14 on the left are of the contralateral and the remaining sections of the ipsilateral lateral geniculate body. The areas containing degenerated boutons are shown in solid black.

of a retino-n. posterior projection from the work of Kingston, Vadas and Bishop (1969). These findings are not absolutely contradictory as the retino-n. posterior projection may be relayed via some other nucleus.

The intermediate cell group of Minkowski consists of islands of cells in the capsule of the L.G.B. in simians. These cells resemble those of the L.G.B. in appearance and might be "displaced" cells from this nucleus. They are known to receive retinal fibres and from their position and appearance these cells appear to be the most obvious homologue of the M.I.N. Although these cells receive a bilateral retinal projection, it is not independent of the retino-geniculate projection as was shown in case Pa 6. Unlike the M.I.N. these cells therefore do not form a mirror image of the L.G.B. and can thus not be regarded as a homologue of the M.I.N. The prosimian Galago crassicaudatus does not help us to establish such a homologue as it has neither a M.I.N. nor an intermediate cell group.

We have been able to demonstrate a retino-pulvinar projection in the three simians studied, but no such projection in the prosimian or pig. It seems especially significant that the area which receives retinal fibres, namely the inferior and lateral border of the inferior pulvinar, is the only part of the pulvinar which does not project to the cortex according to the findings of Walker (1938a) in the

chimpanzee and Peacock and Coombs (1965) in infant rhesus monkeys.

From our findings it would appear that this projection becomes progressively more pronounced during phylogenetic development. This could explain the extensive atrophy of the inferior pulvinar found by Hassler and Wagner (1965) in patients with anophthalmia. On the other hand this could also explain why we were unable to demonstrate a retino-pulvinar projection in Galago crassicaudatus, and why numerous investigators including ourselves, were unable to demonstrate such a projection in various subprimates (Le Gros Clark, 1932; Barris, Ingram and Ranson, 1935; Heyhow, 1958 and 1967; Heyhow et al., 1962; Laties and Sprague, 1966).

It is interesting to note that Ianescu (1969) was able to pick up photic evoked responses in both the New World Saimiri scireus and the prosimian Galago crassicaudatus. In Galago the shortest latency recorded was 38 m.sec. as compared with an average of 14-16 m.sec. for the lateral geniculate body, while in Saimiri the respective latencies were 23 and 12-16 m.sec. The long latent period in the case of the pulvinar seems to point to an indirect propagation of the impulse via some relay nucleus. This finding of Ianescu is very similar to that of Kingston, Vadas and Bishop (1969) concerning the n. posterior of the cat. The suggestion of Pines (1927) that the n. posterior of the cat

should be regarded as part of the pulvinar, therefore remains a distinct possibility.

To conclude, it appears that the retino-pulvinar projection only exists in higher primates as a direct projection. Even in these animals it is a very small projection, when compared with the retino-geniculate projection. From the findings of Hassler and Wagner (1965) it would seem that this projection has developed considerably in man, while we have shown it to be absent in the prosimian Galago crassicaudatus. It must therefore serve a function which becomes important fairly late in phylogeny and is of most importance in man.

The M.I.N., which is a prominent nucleus in the cat and pig, has no homologue in primates. It must therefore serve a function which is of little importance to primates. The above findings concerning the retino-pulvinar projection and the M.I.N. make it very difficult to apply any findings on the visual system, obtained in experiments on cats, to primates or man.

CHAPTER IV

THE PULVINO-CORTICAL PROJECTION IN THE CAT

IV.1 GENERAL

The experimental investigation of the pulvino-cortical projection was restricted to the cat, because this projection has been extensively investigated in primates by numerous authors (Walker, 1935; Le Gros Clark, 1936; Le Gros Clark and Northfield, 1937; Walker, 1938a and 1938b; Chow, 1950; Simpson, 1952; Bucy and Klüver, 1955; and Locke, 1960). These papers will be discussed and the results compared with those obtained by us in the cat.

The pulvino-cortical projection in the cat has not received the same degree of attention. The earliest work, that of Waller and Barris (1937) was a study of the cortical projection of the thalamic nuclei, in which the pulvino-cortical projection occupied but a very small part and was not investigated in any detail. Later, the findings of Sprague (1966) on this projection were incidental to a study of visual, acoustic and somaesthetic deficits after midbrain and cortical lesions. Wilson and Cragg (1967) were primarily concerned with a comparative study of the projection of the lateral geniculate body in the cat and

monkey, and reported on the projection of the pulvinar only as far as their lesions coincidentally involved this latter nucleus.

The present study is therefore the first which is primarily concerned with the pulvino-cortical projection in the cat.

IV.2 MATERIAL AND METHODS

(a) Cats

Twenty five adult female cats with a body weight ranging from 2 Kg. to 2.5 Kg. were used. Female cats in this weight range were selected in an attempt to keep variations to a minimum, as the two atlases used, those of Reinoso-Suàrez (1961) and Snider and Niemer (1961) were both designed for female cats within this weight range.

(b) Instruments

The lesions were made with a Horsley-Clark stereotaxic instrument which had been designed and made by the Department of Physiology of the University of Göttingen.

Stainless steel electrodes with a diameter of 0.5mm at their base were used. The electrodes and the insulating resin were supplied by the firm of Geigy

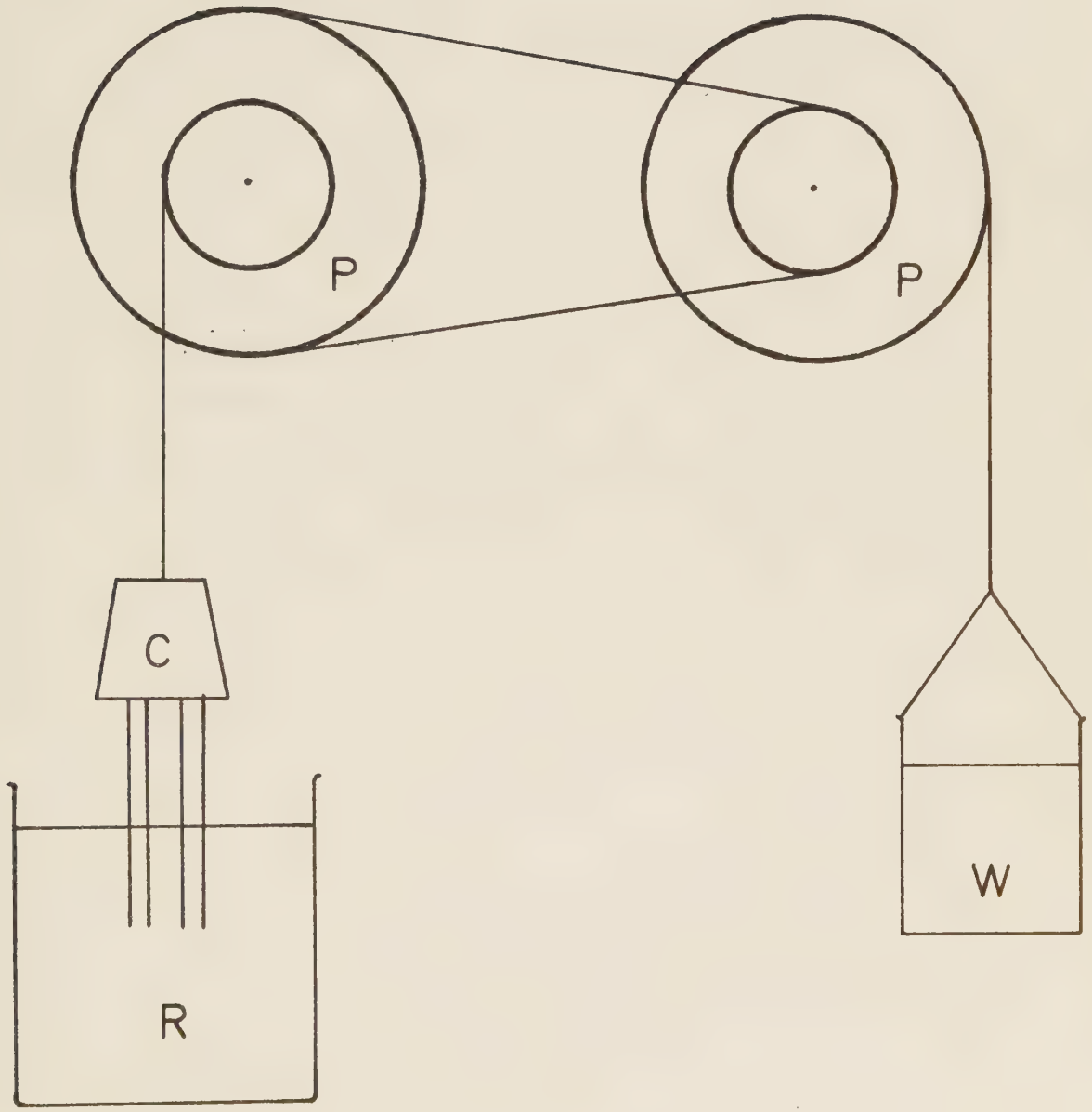


Fig. IV.1

Pulley mechanism for coating electrodes with insulating resin.

Abbreviations: P: pulleys; C: cork R: resin;
W: water.

Pharmaceuticals of Basle. The coating of the electrodes with insulating resin was done by ourselves. For this purpose a simple mechanism was constructed (see fig.IV.1) which consisted of a rubber cork connected, over a number of pulleys, to a counterweight by a cotton thread. As a counterweight a container which could be filled with water was used. The base of an electrode was attached to the rubber cork and so suspended above the resin. The electrode was dipped into the resin and then slowly extracted by the counterweight. The speed of extraction was regulated by altering the friction on the pulley system. It is very important that the electrode is slowly immersed in the resin, as a sudden immersion causes bubbles to form on the side of the electrode. The retraction of the electrode has to be both slow and at an even rate. The slower the rate of removal, the thicker the coat of resin, and uneven retraction causes an uneven coating of the electrode. After each coat of resin the electrode was baked in an incubator at 75^{o}C for 24 hours. It was then examined under a Zeiss operating microscope for any defects. In some cases small air bubbles had entered the resin, and had then expanded and exploded during incubation leaving a small crater. After a sufficiently thick coating of resin had been obtained, usually after 3 to 5 immersions, resin was removed from the tip of the electrode with a surgical blade under an operating microscope. Finally,

before using the electrodes they were tested by immersing them in egg albumen and passing a current through the electrode. At any defective spot in the insulation the albumen would be coagulated.

(c) Anaesthesia and Operation

The animals were anaesthetised with intravenous Nembutal. Their heads were shaved and placed in the headholder of the Horsley-Clark instrument. By adjusting the antero-posterior and lateral co-ordinates, the exact point of entrance was determined with the instrument, and a small craniectomy was then performed in this region, exposing the dura mater. Bleeding from the bone was controlled with bone wax.

The dura mater was not cut, but penetrated by the electrode. This procedure was adopted only after it was found that post-operative cerebral oedema had caused brain herniation through an open dura in the first two cats KPu 1 and KPu 3. This could not be prevented by stitching the dura as it is too thin and friable in the cat to allow successful suturing.

In some cases the electrode approached the pulvinar vertically, and here it entered the cortex at the sulcus lateralis. In other cases the pulvinar was approached

at an angle and the electrode entered the brain at the sulcus suprasylvius or the cortex below it. The point and angle of entrance in each case will be described in the results.

In the first six cats bilateral coagulations were performed and in these cases each hemisphere was numbered. Thus the hemispheres of Cat 1 were numbered KPu 1 and KPu 2 respectively, and so on to cat 6 in which the hemispheres were numbered KPu 11 and KPu 12. Thereafter each serial number refers to one cat in which a unilateral coagulation had been performed.

(d) Perfusion and Removal of Brain

After a post-operative survival period of 7 to 9 days, the cats were perfused with 10% formal saline under Nembutal anaesthesia. This was done in the same way as described for the pig in Chapter III.

After perfusion the top of the skull was removed, anteriorly down to the orbital roof and posteriorly down to the auditory meatus and the attachment of the tentorium cerebelli. The head was then severed at the neck and mounted in the Horsley-Clark instrument.

To be able to cut the brain into blocks along the vertical (frontal) stereotaxic plane, we designed a

knife-holder which could be attached to the instrument in place of the electrode holder. The knife-holder held a surgical blade, with which the brains were cut exactly along the required plane, by manipulating the adjusting screws of the instrument. In this way the brains were cut into three blocks along the vertical stereotaxic plane. The blocks were placed in 10% formol-saline and allowed to post-fix for six weeks.

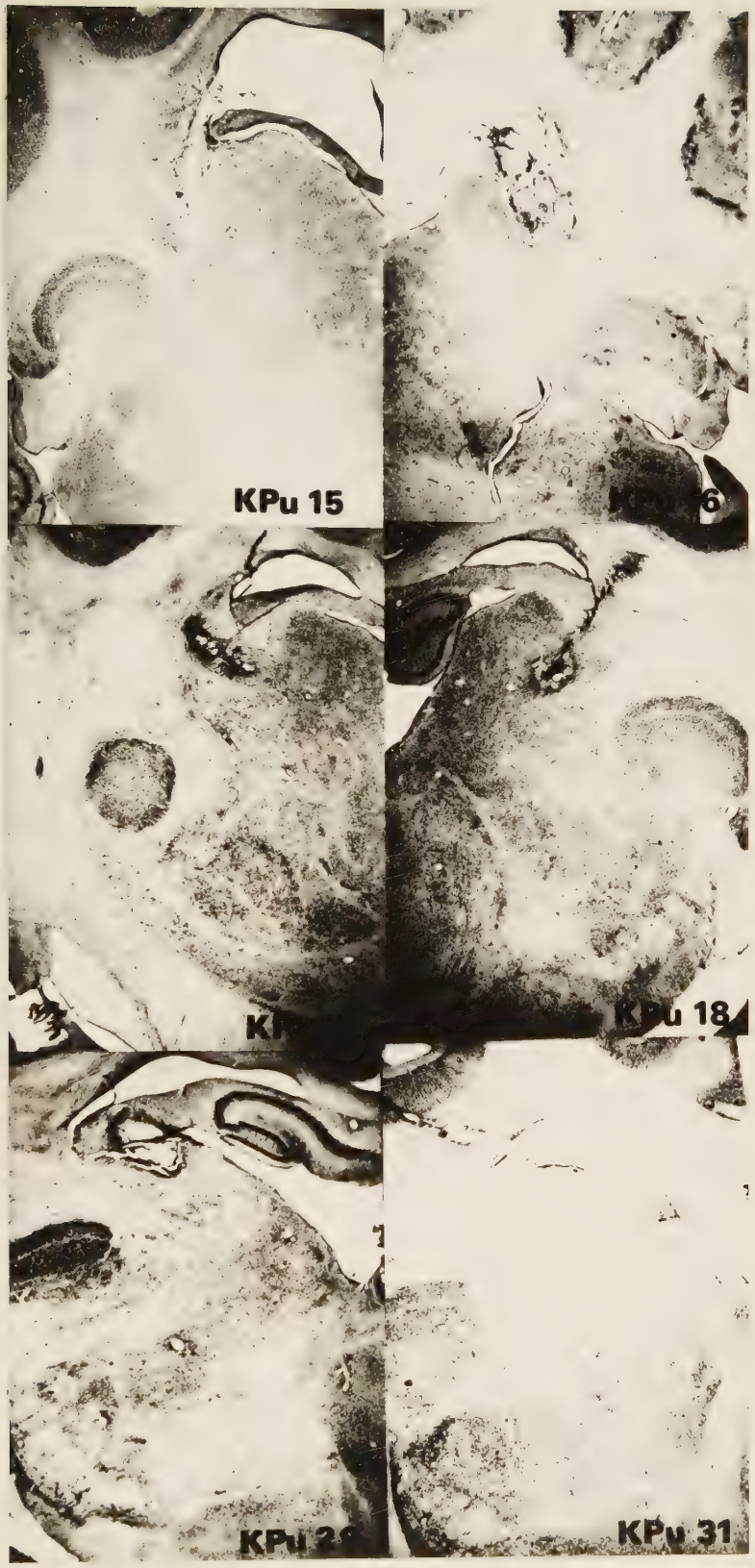
(e) Sectioning and Staining

In all cases serial frozen sections were made. From each brain four comparable series were obtained, three of these consisting of sections 25 microns thick, while the fourth consisted of sections 50 microns thick.

The first two series were stained with the Nauta Gygax (1954) and Fink-Heimer (1967) methods respectively, whilst the third series was kept unstained. The fourth series consisting of the 50microns thick sections was stained with cresyl violet and was used as a topographical control.

(f) Drawings

A normal control cat brain was photographed from the superior, lateral and medial aspects. From these photographs ink line drawings of the brain were made.



Coronal sections of the pulvinar showing the extent of the lesion in six different cats.

Fig. IV. 2.

Before sectioning a brain the exact point of penetration of the electrode was determined in each case, and marked on a line drawing. As the frozen sections were all parallel to the frontal (vertical) stereotaxic plane, each section could be placed by comparing it with one of the atlases used. Thus, when degeneration was observed in a section, it could be related to its correct position on the line drawings of the brain with the help of an atlas. On these drawings the degeneration was represented by dots, the density of which were directly related to the density of distribution of degenerated terminals observed in the cortex.

IV.3 RESULTS

(a) General

The results obtained from 8 of the 23 cats operated on will be described. The other cases were regarded as unsuitable for the following reasons:

(i) Herniation of the Brain

In the first four stereotaxic operations, the dura mater was cut to allow easy penetration of the brain and to avoid deflection of the electrode by the dura.

These cats, however, developed post-operative

oedema of the brain with resultant herniation of brain tissue through the craniotomy. This in turn caused neuronal degeneration in the affected cortex, as well as degeneration of numerous cortico-cortical fibres, with the result that the material was worthless for this investigation.

(ii) Bilateral Coagulation

Only after examining our control material did we see how much degeneration an electrode tract alone could cause. As the electrode severs both direct and commissural cortico-cortical fibres, we felt that in cases with bilateral lesions there would be too much artifact to allow a critical evaluation.

(iii) Malposition and excessive Size of Lesion

In many cases the pulvinar was missed completely. The degree of accuracy was not very high as all cat atlases are designed for an idealised "standard cat" weighing 2.5 Kg. and no allowances are made for individual variations. Furthermore, although the position of the electrode could be checked electrophysiologically, within certain limits, this was of no help as one cannot repeat the attempt on the same animal due to the damage caused by the electrode

Fig. IV.3

The diagram shows the superior lateral and medial aspects of the left hemisphere of Cat KPu 14.

The distribution of degenerated fibres is shown by dots and solid black areas. The density of the dots indicates the density of distribution of terminally degenerated fibres. The areas which contained the greatest number of degenerated fibres are shown in solid black. The point of entrance of the electrode is marked by a large black dot situated on the lateral sulcus.

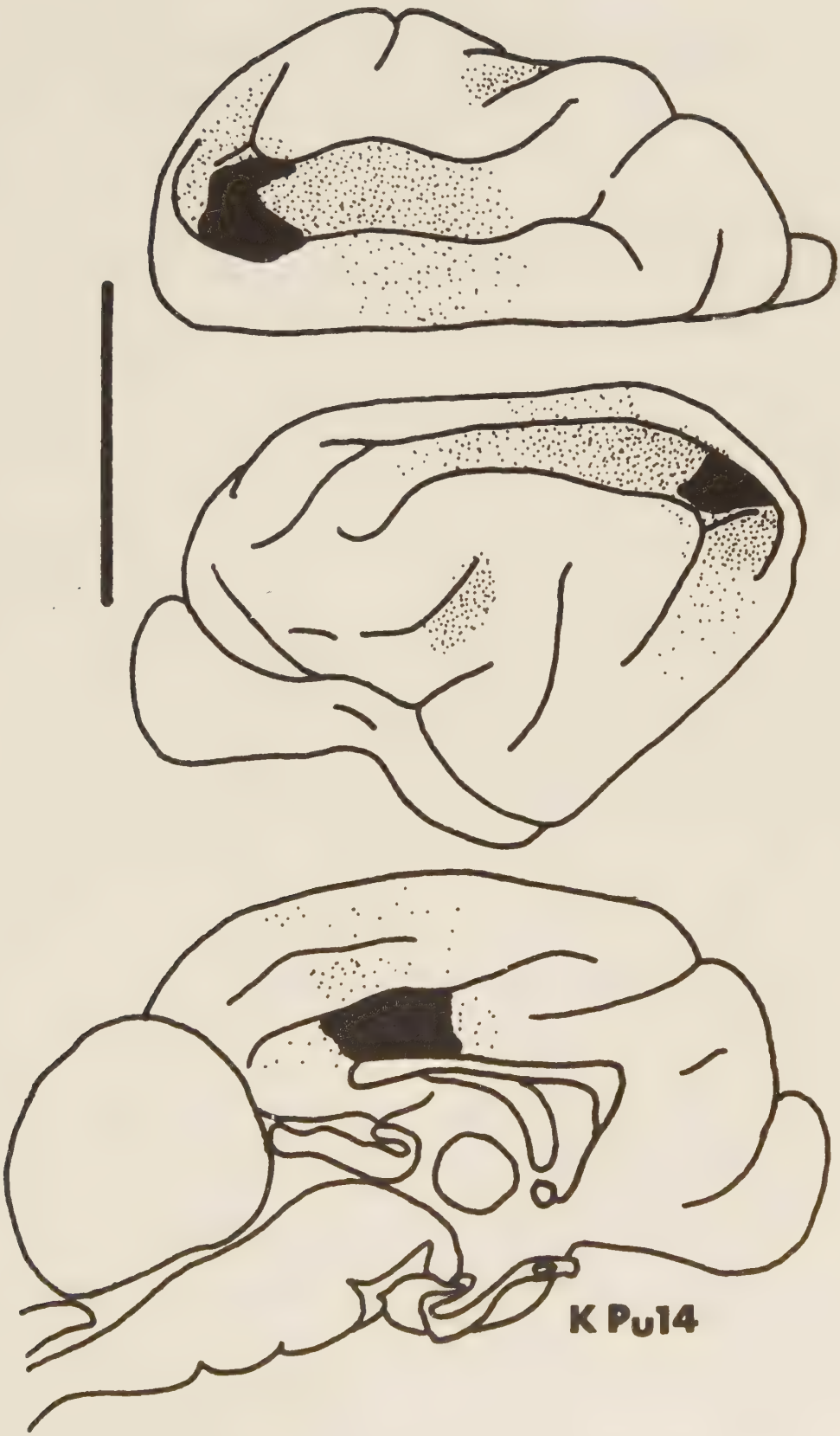


Fig. IV.3

tract. The exact position of the lesion is unfortunately only discovered after the brain has been sectioned and stained.

In other cases the lesion was far too large, as was the case in KPu 6 where the lesion involved the greater part of the posterior thalamus and meta-thalamus. Similar large lesions were also found in cases KPu 8, KPu 22 and KPu 25.

(b) Cat KPu 14

In this case the electrode entered the cortex vertically through the lateral sulcus in the frontal plane +6.5. The lesion involved the posterior part of the pulvinar and was fairly large. Its extent along the Horsley-Clark planes was as follows:

Horizontally from +5 to +8

Antero-posteriorly from +6.5 to +7.5

Laterally from 6 to 6.5

The distribution of terminal degeneration in the cortex is shown in figure IV.3. The pattern closely resembled that seen in the next two cases, KPu 15 and KPu 16, in which adjacent parts of the pulvinar were coagulated.

(i) Gyrus Suprasylvius

For descriptive purposes this gyrus was

divided into anterior, middle and posterior divisions, corresponding to the subdivisions of the ectosylvian gyri.

The greatest number of terminally degenerated fibres were found in this gyrus. The anterior part showed only minimal terminal degeneration, but the density of degenerated fibres increased considerably in the middle part, and reached its maximum in the posterior division. The densest distribution of terminal degeneration was found anteriorly in the posterior division, the density decreasing further posteriorly. This can be seen best in the superior view of the brain (fig. IV.3) as the true appearance is somewhat obscured by the convexity of the brain in the lateral view. The dense pattern of degeneration continued into the lateral sulcus as far as the medial end of the trough of the sulcus. At the junction of the medial wall with the trough the pattern of degeneration changed abruptly, and the medial wall of the lateral sulcus contained only sparsely distributed degenerated fibres.

(ii) Gyrus lateralis

Sparsely distributed degenerated fibres were

present in the middle part of this gyrus, the rest of the gyrus being completely free from degeneration. When the brain is viewed from above (fig.IV.3), it will be seen that the degeneration in this gyrus forms half of a circle, of which the centre is the entrance point of the electrode.

(iii) Gyrus Ectosylvius

A fairly dense island of degeneration was present in this gyrus, extending anteriorly into the gyrus sylvius anterior. This island of degeneration was confined to the anterior-inferior part of the gyrus ectosylvius medius, leaving the rest of the gyrus ectosylvius medius as well as the anterior and most of the posterior ectosylvian gyri free from degeneration. In the posterior tip of the posterior ectosylvian gyrus a few degenerated fibres were seen.

(iv) Gyrus Parasplenialis

Very densely distributed degenerated fibres were observed in the middle part of the gyrus. The pattern of degeneration changed quite abruptly to become very sparse and disappeared completely anterior and posterior to the middle part. This is clearly shown on the medial view of the brain

in figure IV.3.

(v) Gyrus Suprasplenialis

Sparsely distributed degenerated fibres were seen in the middle part of this gyrus.

(c) Cat KPu 15

In this case the electrode entered the cortex through the suprasylvian sulcus in the frontal plane +6. The coagulation destroyed the lateral half of the pulvinar and encroached upon the medial half (see fig.IV.2). The extent of the lesion along the Horsley-Clark planes was as follows:

Horizontally from +5 to +8

Antero-posteriorly from +5.5 to +8.5

Laterally from 6 to 8

The complete antero-posterior extent of the pulvinar (AP+5.5 to AP+8.5) was therefore involved including the hilar region and part of the pedunculus thalamicus superior. The pattern of termination of degenerated fibres in the cortex is shown in figure IV.4.

(i) Gyrus Suprasylvius

This gyrus contained the greatest number of

Fig. IV.4

The diagram shows the superior lateral and medial aspects of the right hemisphere of cat KPu 15.

The distribution of degenerated fibres is shown by dots and solid black areas. The density of the dots indicates the density of distribution of terminally degenerated fibres. The areas which contained the greatest number of degenerated fibres are shown in solid black. The point of entrance of the electrode is marked by a large black dot situated on the suprasylvian sulcus.

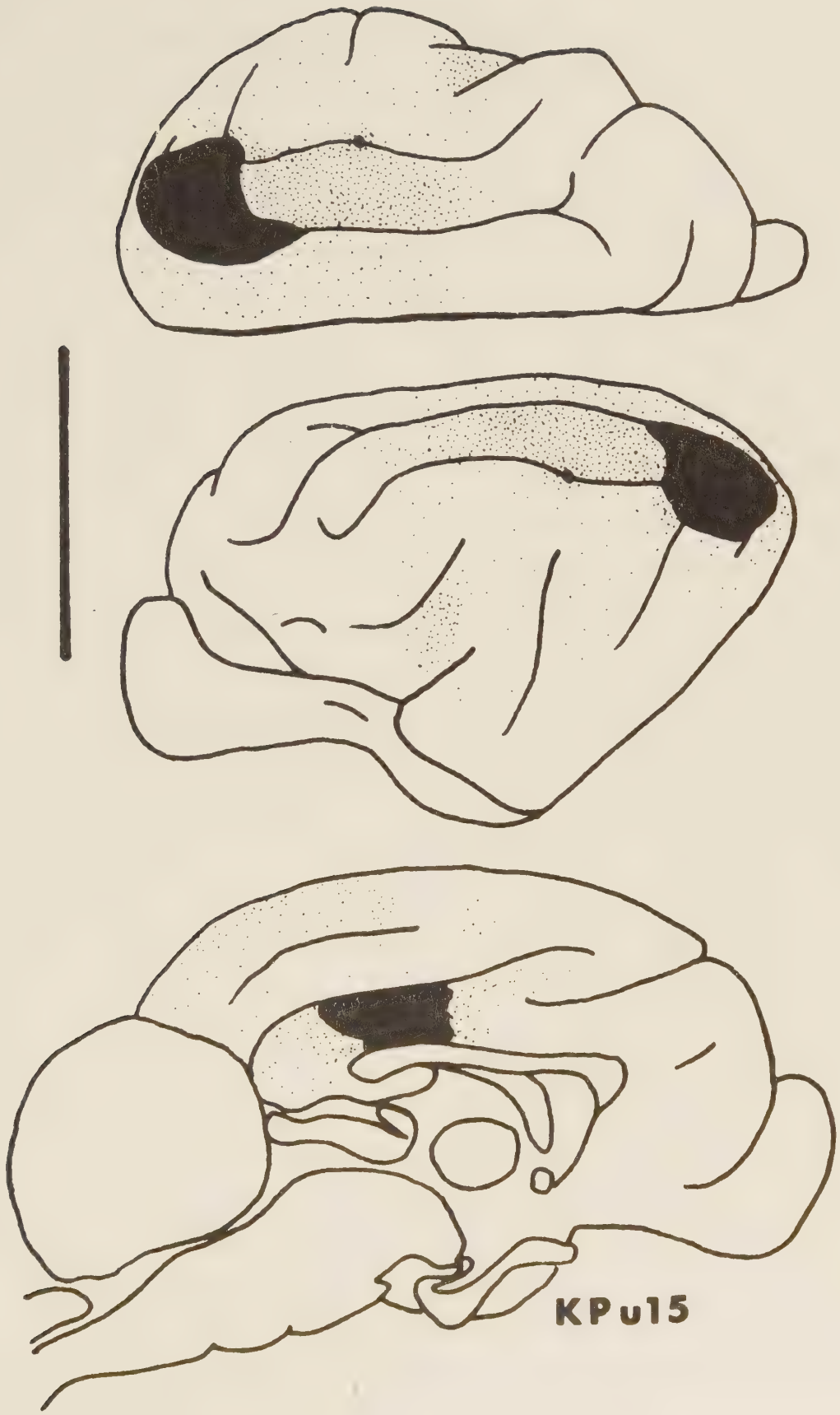


Fig. IV.4

degenerated fibres. The distribution pattern of these fibres was as follows:

The anterior part of the gyrus contained hardly any degenerated fibres and the few that were present were found at the junction of the middle and anterior divisions. Quite a substantial number of degenerated fibres were found in the middle division. It became evident that the density of distribution increased progressively further posteriorly along the gyrus. This can also be seen in figure IV.4. The highest concentration of degenerated fibres was found in the posterior division of the suprasylvian gyrus. The dense degeneration extended further posterior than in the previous case (KPu 14), in which the lesion also extended further posteriorly (+5.5 in KPu 15 compared with +6.5 in KPu 14). Laterally the degeneration extended as far as the suprasylvian culcus, where the density of distribution rapidly diminished down the medial wall of the sulcus. Medially the degeneration extended into the lateral sulcus. The density of distribution remained constant up to the junction of the medial wall with the trough where it changed abruptly. The density of distribution of degenerated fibres

Fig. IV.5

The diagram shows the superior lateral and medial aspects of the left hemisphere of cat KPu 16.

The distribution of degenerated fibres is shown by dots and solid black areas. The density of distribution of terminally degenerated fibres is indicated by the density of the dots. Areas containing the greatest number of degenerated fibres are shown in solid black. The point of entrance of the electrode is indicated by a large black dot situated on the lateral sulcus.

Fig. IV.5

in the medial wall was the same as found in the lateral gyrus.

(ii) Gyrus Lateralis

Only sparsely distributed degenerated fibres were seen in this gyrus. The anterior-posterior extent of the degeneration was very much like that of the degenerated fibres in the suprasylvian gyrus. The density however showed no signs of increasing further posteriorly, as was the case in the suprasylvian gyrus, but remained fairly constant throughout the extent of the degeneration.

(iii) Gyrus Ectosylvius

A concentration of degenerated fibres was present in the anterior-inferior corner of the middle ectosylvian gyrus, extending into part of the anterior sylvian gyrus. Occasional single degenerated fibres were seen in the anterior and posterior ectosylvian gyri as well as in the posterior superior part of the middle ectosylvian gyrus. A small concentration of degenerated fibres again occurred in the extreme posterior corner of the posterior ectosylvian gyrus.

(iv) Gyrus Parasplenialis

Densely distributed degenerated fibres were seen in the middle part of the parasplenial gyrus. Anterior and posterior to this part of the gyrus the number of degenerated fibres diminished rapidly.

(v) Gyrus Suprasplenialis

Occasional single degenerated fibres occurred in the middle and posterior parts of this gyrus.

(d) Cat KPu 16

In this case the electrode entered the cortex vertically through the lateral sulcus in the frontal plane +6. The lesion involved the complete ventro-dorsal extent of the nucleus. Unlike the previous case the fibres of the pedunculus thalamicus superior were not involved. The extent of the lesion along the Horsley-Clark planes was as follows:

Horizontally from +5 to +8

Antero-posteriorly from +5 to +8

Laterally from 6 to 8

The pattern of termination of degenerated fibres is shown in figure IV.5.

(i) Gyrus Suprasylvius

In comparison with other gyri, this gyrus

contained the largest number of degenerated fibres. The density of degenerated fibres increased progressively from anterior to posterior, the maximum density being reached just before the angle of the gyrus. Unlike KPu 15, but similar to KPu 14, degenerated fibres were distributed far down the lower limb of this gyrus (fig.IV.5). Laterally the degeneration stopped at the supra-sylvian sulcus and medially it continued into the lateral sulcus as far as its medial wall. The same abrupt change in pattern of degeneration, described previously, was present at the junction of the trough of the sulcus with its medial wall.

(ii) Gyrus Lateralis

A fair number of degenerated fibres were seen in this gyrus. As can be seen in figure IV.5. these degenerated fibres were not distributed over the complete width of this gyrus. The anterior part of the gyrus was free from degenerated fibres except at its junction with the middle part. The middle part contained the largest number of degenerated fibres, which also extended over the complete width of the gyrus opposite the point of entrance of the electrode. In the posterior part of the gyrus the degenerated fibres formed only a

narrow band along the lateral sulcus.

(iii) Gyrus Ectosylvius

The anterior ectosylvian gyrus was free from degenerated fibres. The middle ectosylvian gyrus contained a dense patch of degenerated fibres in its anterior-inferior corner. This area of degeneration continued antero-inferiorly for a short way into the gyrus sylvius anterior. In the remaining part of the middle ectosylvian gyrus occasional degenerated fibres were seen. The posterior ectosylvian gyrus contained a concentration of degenerated fibres in its posterior corner. In the remaining extent of this gyrus, occasional degenerated fibres were seen.

(iv) Gyrus Parasplenialis

A fair number of degenerated fibres were seen in the middle third of this gyrus. A few degenerated fibres were present for a short distance anterior and posterior to this middle section.

(v) Gyrus Suprasplenialis

Sparsely distributed degenerated fibres were seen in the middle part of this gyrus.

Fig. IV.6

The diagram shows the superior lateral and medial aspects of the right hemisphere of cat KPu 17.

The distribution of degenerated fibres is shown by dots and solid black areas. The density of distribution of terminally degenerated fibres is indicated by the density of the dots. Areas containing the greatest number of degenerated fibres are shown in solid black. The point of entrance of the electrode is indicated by a large black dot on the suprasylvian sulcus.

Fig. IV.6

(e) Cat KPu 17

In this case the electrode entered the cortex at an angle of 30° through the suprasylvian sulcus in the frontal plane +8.5. The lesion was large and involved the oral end of the pulvinar as well as the greater part of the nucleus lateralis dorsalis. The lesion also extended into the fibres of the pedunculus thalamicus superior (fig.IV.2). The extent of the lesion along the Horsley-Clark planes was as follows:

Horizontally from +5 to +7

Antero-posteriorly from +7.5 to +10

Laterally from 4 to 6

The pattern of termination of degenerated fibres is shown in figure IV.6.

(i) Gyrus Suprasylvius

This gyrus contained a large number of densely distributed degenerated fibres which were mainly confined to its middle section. As can be seen in figureIV.6 this area of degeneration continued for a short distance into the anterior and posterior parts of the gyrus leaving most of the anterior and posterior sections free from degenerated fibres. Medially the degenerated fibres continued into the lateral sulcus as far as the junction of the

trough with the medial wall.

(ii) Gyrus Lateralis

Sparsely distributed degenerated fibres were seen in the middle part of this gyrus. The degenerated fibres also extended into the anterior and posterior parts for a short way. The anterior-posterior extent of the degeneration was therefore the same as that in the suprasylvian gyrus. The density of the degeneration decreased from lateral to medial. Along the posterior half of the middle section and in the posterior section the area of degeneration did not reach the midline (fig.IV.6).

(iii) Gyrus Ectosylvius

A small number of degenerated fibres were seen in the anterior ectosylvian gyrus immediately below the point of entrance of the electrode. A small concentration of degenerated fibres was present in the anterior inferior corner of the gyrus ectosylvius medius, leaving the rest of this gyrus free from degenerated fibres. This area of degeneration continued into the gyrus sylvius anterior for a short distance. Degenerated fibres were seen in the posterior corner of the gyrus ectosylvius posterior.

(iv) Gyrus Parasplenialis

In this case the maximal concentration of degenerated fibres was found in the parasplenial gyrus, thereby distinguishing it from the previous cases where the maximal concentration of degenerated fibres was found in the suprasylvian gyrus. The degenerated fibres were spread over part of the anterior, the middle and most of the posterior divisions of the gyrus. The density of degeneration again decreased both anteriorly and posteriorly.

(v) Gyrus Suprasplenialis

Sparsely distributed degenerated fibres were seen in the middle part of this gyrus, while no degenerated fibres were seen in the anterior or posterior sections.

(f) Cat KPu 18

In this case the electrode entered the cortex through the suprasylvian sulcus at an angle of 30°. The lesion was small and round, involving the middle and anterior part of the pulvinar and encroaching slightly upon the upper part of the pedunculus thalamicus superior (fig.IV.2). The extent of the lesion along

Fig. IV.7

The diagram shows the superior, lateral and medial aspects of the left hemisphere of cat KPu 18.

The distribution of degenerated fibres is shown by dots and solid black areas. The density of the dots indicates the density of distribution of terminally degenerated fibres. Areas containing the greatest number of degenerated fibres are shown in solid black. The point of entrance of the electrode is indicated by a large black dot on the suprasylvian sulcus.

Fig. IV.7

the Horsley-Clark planes was as follows:

Horizontally from +5 to +6

Antero-posteriorly from +6 to +7

Laterally from 6 to 7

The pattern of distribution of degenerated fibres is shown in figure IV.7.

(i) Gyrus Suprasylvius

This gyrus contained the largest number of degenerated fibres. Its anterior part was free of degeneration. In the middle part the density of degeneration increased from sparse at the anterior end to very dense at the posterior end. The posterior part of the gyrus contained densely distributed degenerated fibres in its anterior half, the density of the fibres diminishing further posteriorly. It should be noted that the area of maximum density of degeneration projected in a tongue anteriorly towards the point of penetration of the electrode (fig.IV.7). Densely distributed degeneration was seen in the lateral wall and trough of the lateral sulcus.

(ii) Gyrus Lateralis

Very sparsely distributed degenerated fibres were seen in the middle and posterior parts of

this gyrus. The density of distribution increased along the lateral border of the gyrus.

(iii) Gyrus Ectosylvius

The gyrus ectosylvius anterior was free from degenerated fibres. In the gyrus ectosylvius medius a small concentration of degenerated fibres was present in its anterior-inferior corner. This area of degeneration continued into the gyrus sylvius anterior for a short distance. In the remainder of the gyrus ectosylvius medius occasional degenerated fibres were seen. The gyrus ectosylvius posterior contained a few degenerated fibres in its posterior corner.

(iv) Gyrus Parasplenialis

A fair number of degenerated fibres were seen in the middle part of this gyrus. Immediately anterior and posterior to the middle section a very small number of degenerated fibres were present.

(v) Gyrus Suprasplenialis

Occasional degenerated fibres were seen in the middle part of this gyrus.

Fig. IV.8

The diagram shows the superior, lateral and medial aspects of the right hemisphere of cat KPu 28.

The distribution of degenerated fibres is shown by dots, the density of which indicates the density of distribution of terminally degenerated fibres. The point of entrance of the electrode is indicated by a large black dot in the middle of the suprasylvian gyrus.

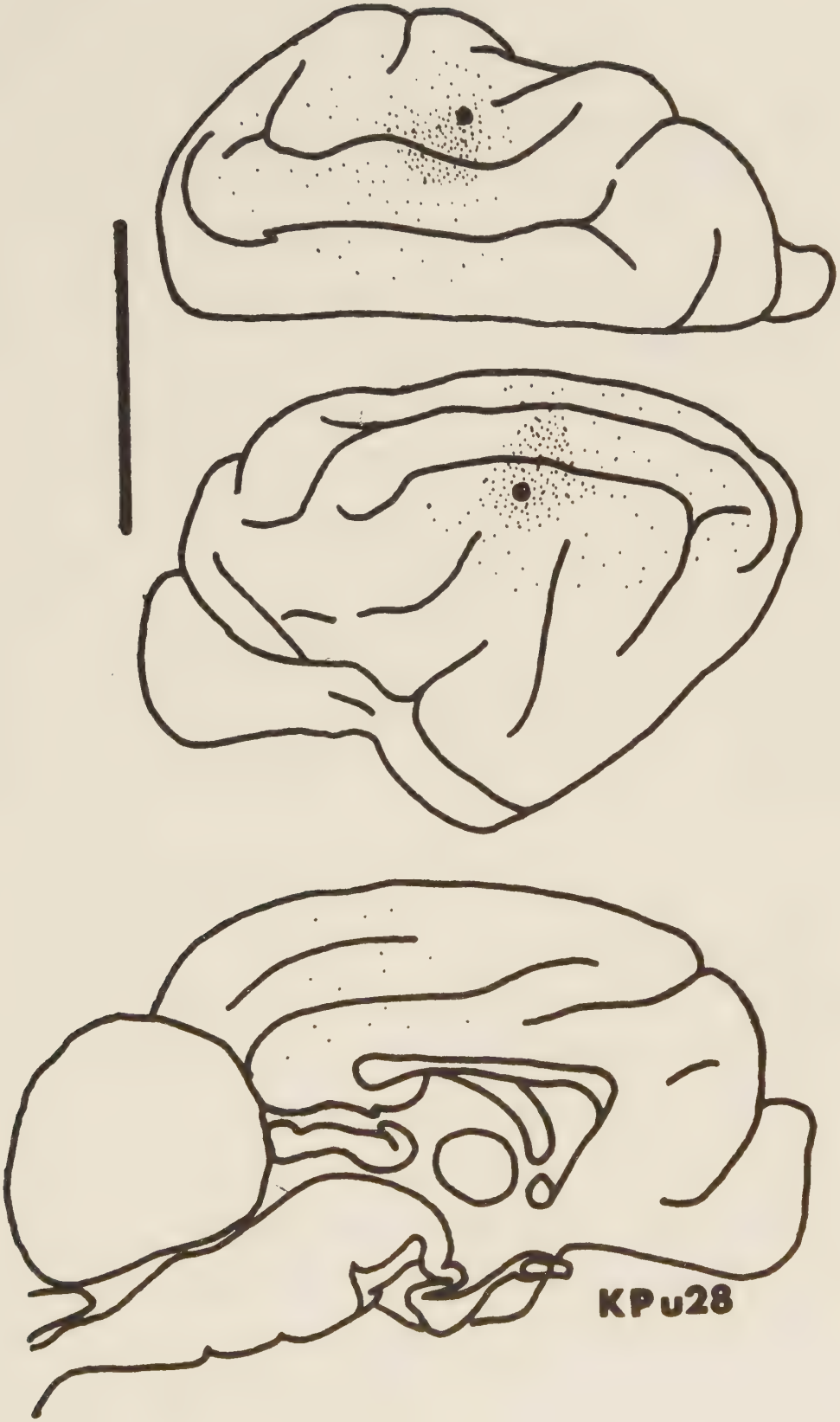


Fig. IV.8

(g) Cat KPu 28

In this case the electrode penetrated the cortex at an angle of 30° immediately below the suprasylvian sulcus in the gyrus ectosylvius medius. The lesion was small and involved the fornix and part of the thalamic radiation (fig.IV.2), without affecting the pulvinar. The extent of the lesion along the Horsley-Clark planes was as follows:

Horizontally from +3.5 to +4.5

Antero-posteriorly from +6.5 to +7.5

Laterally from 5.5 to 7.0

The distribution of the degenerated fibres is shown in figure IV.8.

(i) Gyrus Suprasylvius

Degenerated fibres were concentrated along the lateral border of the middle part of the gyrus. This concentrated area of degeneration formed part of the roughly circular area of degeneration which surrounded the point of entrance of the electrode, as can be seen in figure IV.8. Otherwise occasional degenerated fibres were seen in the middle division and the anterior part of the posterior division of this gyrus.

(ii) Gyrus Lateralis

A few single degenerated fibres were found

in the middle part of this gyrus.

(iii) Gyrus Ectosylvius

A concentration of degenerated fibres was seen in the upper part of the gyrus ectosylvius medius immediately surrounding the point of entrance of the electrode. The concentration of degenerated fibres diminished rapidly further away from the point of entrance. The anterior-inferior corner, which contained degenerated fibres in all the previous cases, was completely free from degeneration in this case. Occasional degenerated fibres were seen in the upper parts of the anterior and posterior ectosylvian gyri.

(iv) Gyrus Parasplenialis

A very small number of single degenerated fibres were seen in the middle part of this gyrus.

(v) Gyrus Suprasplenialis

Very few single degenerated fibres were seen in the middle part of this gyrus.

(h) Cat KPu 29

The electrode entered the cortex at an angle of

Fig. IV.9

The diagram shows the superior, lateral and medial aspects of the right hemisphere of cat KPu 29.

The distribution of degenerated fibres is shown by dots, the density of which indicates the density of distribution of terminally degenerated fibres. The point of entrance of the electrode is indicated by a large black dot on the suprasylvian sulcus.

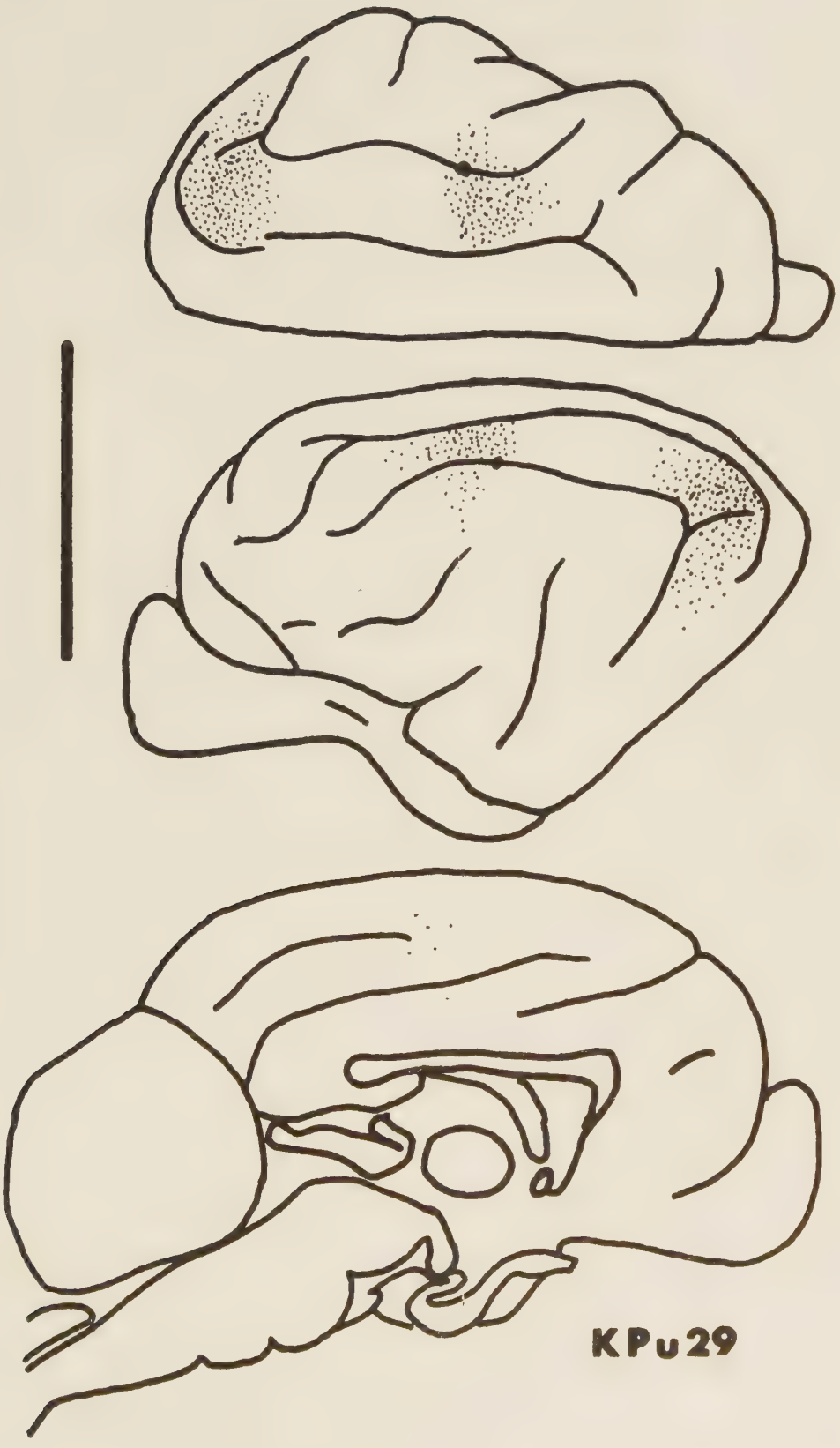


Fig. IV.9

30° through the suprasylvian sulcus. The lesion was small and involved the dorsal part of the pulvinar towards its posterior end, completely sparing the pedunculus thalamicus superior. The lesion did however involve the fornix (fig.IV.2). The extent of the lesion along the Horsley-Clark planes was as follows:

Horizontally from +7 to +8

Antero-posteriorly from +4.5 to +5.5

Laterally from 6 to 7

The pattern of distribution of the degenerated fibres can be seen in figure IV.9. It should be noted that although the electrode entered the cortex quite far anteriorly, the coagulation affected the posterior end of the pulvinar (fig.IV.2). The electrode must therefore have been angled or deflected posteriorly.

(i) Gyrus Suprasylvius

Degenerated fibres were concentrated in the anterior third, and the anterior tip of the middle third of this gyrus. This concentration of degenerated fibres were immediately adjacent to the point of penetration of the electrode. Most of the middle part of this gyrus was free from degenerated fibres. The posterior part contained a large number of degenerated fibres, the maximum

concentration being found in the elbow of the gyrus. The degeneration in the posterior part continued medially into the lateral sulcus as far as the medial wall of the sulcus where it stopped abruptly. The degeneration in the anterior part of this gyrus stopped a small distance from the lateral sulcus as can be seen in the superior view of the brain in figure IV.9.

(ii) Gyrus Lateralis

No degenerated fibres were seen in this gyrus.

(iii) Gyrus Ectosylvius

In the gyrus ectosylvius anterior a small area of degenerated fibres was seen immediately adjacent to the point of entrance of the electrode. The remaining extent of this gyrus and the middle and posterior ectosylvian gyri were completely free from degenerated fibres.

(iv) Gyrus Parasplenialis

No degenerated fibres were seen in this gyrus.

(v) Gyrus Suprasplenialis

A few single degenerated fibres were seen

Fig. IV.10

The diagram shows the superior, lateral and medial aspects of the right hemisphere of cat KPu 31.

The distribution of degenerated fibres is shown by dots, the density of which indicates the density of distribution of terminally degenerated fibres. The point of entrance of the electrode is indicated by a large black dot in the middle of the suprasylvian gyrus.

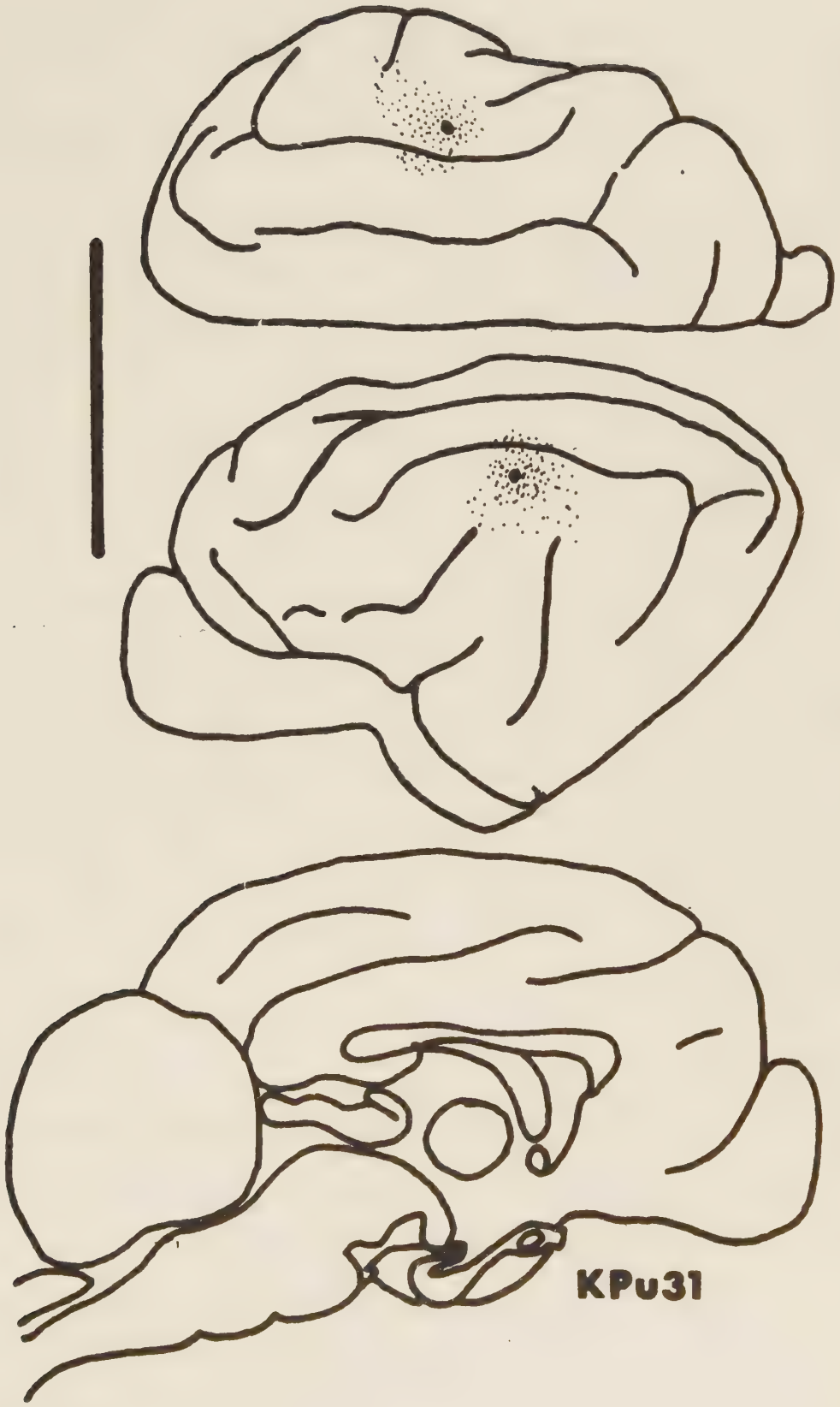


Fig. IV.10

in the middle part of this gyrus.

(i) Cat KPu 31

In this case the electrode entered the cortex at an angle of 30°, immediately below the suprasylvian sulcus, in the gyrus ectosylvius medius. No coagulation was made. The electrode tract can be seen passing through the fornix into the dorsal surface of the pulvinar in figure IV.2.

Degenerated fibres were seen only in the immediate vicinity of the point of penetration of the electrode (fig.IV.10). They were therefore confined to the upper part of the gyrus ectosylvius medius as well as a small crescent shaped area on the lateral border of the middle part of gyrus suprasylvius. All other gyri were free from degenerated fibres.

IV.4 DISCUSSION

(a) Problems related to the Method of Investigation

The particular advantage of the stereotaxic method is that it allows exploration of the deep lying structures of the brain. Unfortunately the method also has some disadvantages, namely, the damage caused by the electrode tract, the inaccuracy of the method, and the unselective nature of the lesion. These disadvantages have to be

taken into account before a critical appraisal of the results can be made.

(i) The Electrode Tract

On its way through the cortex to the pulvinar the electrode damages fibres not derived from the pulvinar. To distinguish the resulting degeneration from that caused by the lesion of the pulvinar, case KPu 31 was included in the investigation. In this cat the electrode was implanted, but no coagulation was made. The resulting degeneration was localised immediately around the point of entrance of the electrode. Degeneration around the point of entrance must therefore be regarded as artifact or at least partly artifact. In case KPu 29 artifact can easily be distinguished from pulvino-cortical degeneration because the two areas were separated by a degeneration-free zone. On the other hand, artifact and pulvino-cortical degeneration may overlap to such an extent as to be indistinguishable as occurs in case KPu 17. However, once the size and density of the artifact degeneration is known, it poses no great problem in the interpretation of the results.

(ii) The Inaccuracy of this Method

Because of individual variations, the nucleus

can easily be missed as was the case in 20 of the 30 attempts. The position of the electrode can be determined to some extent electrophysiologically, but as two or even three attempts at placing the electrode in the same animal would cause too much artifact, this is not of much help. To ensure a certain degree of success a large number of animals was used. Thus, in spite of the method having only a 30 per cent success rate, we still obtained sufficient usable material.

The size and shape of the lesion is even more difficult to control than its position.

In a number of cases the lesion extended into the fornix and part of the thalamic radiation. As the fornix does not project to the cortex a lesion of the fornix was not considered to contribute to the artifact. A lesion in the thalamic radiation could, however, cause a considerable amount of artifact. For this reason case KPu 28 was used as a control in which the fornix and part of the thalamic radiation were coagulated. The resulting degeneration was spread over a far wider area than in the other control animal, KPu 31. These findings will be taken into consideration in the interpretation of the results.

(iii) The Composition of the Pulvinar

Unfortunately, from our point of view, the pulvinar is composed of cells and fibre bundles like most other nuclei. These fibre bundles are not all derived from cells of the pulvinar, but are mostly fibres passing through the pulvinar. Such fibre tracts include the retino-tectal fibres (described in Chapter III) and the cortico-tectal fibres (described in Chapter V). These tracts are naturally involved in any lesion of the pulvinar as coagulation cannot selectively destroy the cells. The destruction of such fibre bundles could cause a considerable amount of artifact. In interpreting the results, the contribution of such artifact to the general picture can be excluded by comparing our findings with those obtained by the method of retrograde degeneration.

(b) Distribution of the Pulvino-cortical Fibres

(i) The Visual Area

Mapping of the visual area of the cat was undertaken physiologically in 1941 by Talbot and Marshall. By stimulating the retina with small spots of light, and recording the cortical evoked potentials, they mapped out, in each hemisphere of the cat cortex, two topographic projections of the

contralateral visual field. The more medial area was termed "visual area I", while the lateral area was termed "visual area II". Visual area I corresponded more or less to the striate cortex whereas the visual area II had no clear cyto-architectural correlation.

The exact position of boundaries of areas 17, 18 and 19 of the cat were defined for the first time by Otsuka and Hassler (1962). The designations 17, 18 and 19 refer to anatomically defined regions.

In an extensive investigation of the visual areas of the cat, Hubel and Wiesel (1965) physiologically detected a third visual area which they called "visual area III". This area is distinct from and lies lateral to visual area II of Talbot and Marshall (1941). In addition to the physiological study, Hubel and Wiesel (1965) also studied the visual cortex of the cat histologically using Nissl, Myelin and Nauta stained sections. They found an absolute correlation between the physiological visual areas (I, II and III) and the anatomical regions 17, 18 and 19.

Area 17 (visual area I) occupies the posterior

part of the lateral gyrus. Part of area 17 does however extend over the dorsal surface of the brain and occupies from a quarter to a third of the lateral gyrus depending on the antero-posterior level. More posteriorly the area involved becomes wider. The boundary between areas 17 and 18 appears to be particularly prone to individual variations which probably accounts for the differences in position assigned to it by various neuroanatomists (Minkowski, 1913; Otsuka and Hassler, 1962; Hubel and Wiesel, 1965). The boundary between areas 18 and 19 is at the trough of the lateral sulcus. Area 19 occupies the complete width of the suprasylvian gyrus. The visual areas are confined to the posterior division of the suprasylvian and lateral gyri and the more posterior part of the middle division.

Area 17

In both KPu 16 and KPu 17, area 17 was quite free of degenerated fibres. In these two cases the boundary between areas 17 and 18 was clearly visible. In both cases fairly dense degeneration was present in the lateral part of the gyrus lateralis (area 18), whereas the medial part was free from degenerated fibres. Moreover the degeneration-free area becomes wider further

posteriorly, which corresponds with the description of area 17 by Otsuka and Hassler (1962) and Hubel and Wiesel (1965).

In cases KPu 14 and KPu 29 no degenerated fibres were found in areas 17 and 18.

In case KPu 18 degenerated fibres were present in the lateral gyrus, their density decreasing from lateral to medial. In this case it was difficult to define the boundary between areas 17 and 18 exactly. If however we assume that it was in the same position as in cases KPu 16 and KPu 17, which is the typical position according to Otsuka and Hassler (1962) and Hubel and Wiesel (1965), then there are a few single degenerated fibres present in area 17. We feel that these degenerated fibres are probably due to coagulation of part of the pedunculus thalamicus superior.

Finally in case KPu 15 the complete width of gyrus lateralis posterior contained degenerated fibres. The density of the degenerated fibres remained constant from lateral to medial and only started to decrease on the medial side of the hemisphere. It is significant that, in this case, the lesion in the pulvinar was larger than in any

other case, destroying the greater part of the nucleus. The degeneration seen in area 17 in this case is therefore probably due to fibres of passage through the pulvinar which had been destroyed by the coagulation. Additionally it is also possible that the boundary between areas 17 and 18 is more medial in KPu 15 than it was in the other cases.

We therefore conclude that area 17 as defined by Otsuka and Hassler (1962) and which is identical to the physiologically defined visual area I, (Talbot and Marshall, 1941; Hubel and Wiesel, 1965) receives no projection from the pulvinar in the cat.

Area 18

In all cases except KPu 14 and KPu 29 a significant number of degenerated fibres were seen in area 18. The degenerated fibres were less densely distributed than in the adjacent suprasylvian gyrus, and the boundary between areas 18 and 19, in the sulcus lateralis, was well defined in all cases.

In case KPu 14 degenerated fibres were seen in the lateral gyrus, but mostly anterior to area 18. These degenerated fibres formed part of a circle

of degeneration surrounding the point of entrance of the electrode.

In case KPu 29 where the point of penetration was further lateral in the suprasylvian sulcus the surrounding area of degeneration did not extend into the lateral gyrus, but remained confined to the suprasylvian and anterior ectosylvian gyri. In both cases, KPu 14 and KPu 29, in which there was no degeneration in area 18 the lesion in the pulvinar was small and confined to the dorsal surface of the pulvinar.

It therefore seems likely that the dorsal part of the pulvinar does not project to the lateral gyrus (or area 18).

From these findings we conclude that there is a projection from the pulvinar to area 18.

Area 19

Densely distributed degenerated fibres were seen in area 19 in all cases. The maximum concentration of degenerated fibres was in the posterior part, or elbow, of the suprasylvian gyrus, but many degenerated fibres were also seen in the middle part of this gyrus.

This partly confirms the findings of Waller and Barris (1937) who found retrograde degeneration in the pulvinar after lesions of the caudal part of the middle suprasylvian gyrus. Retrograde degeneration in the pulvinar was also seen by Sprague (1966) after lesions of the postero-middle suprasylvian gyrus.

Medially the densely distributed degenerated fibres extended as far as the junction between the trough and medial wall of the lateral sulcus. This coincides with the medial boundary of area 19.

The projection to the suprasylvian gyrus appeared to be topographically organised, in so far as the caudal part of the pulvinar projected to the caudal part of the gyrus suprasylvius. The nucleus lateralis posterior, which lies immediately anterior to the pulvinar, projected to gyrus suprasylvius immediately anterior to the projection area of the pulvinar. This is best seen by comparing cases KPu 16 and KPu 17.

The cortical projection in case KPu 16, with the most caudal coagulation, was to the posterior division of gyrus suprasylvius (fig.IV.5). The coagulation in case KPu 17 was the most anterior

of all and involved the oral end of the pulvinar and part of the nucleus lateralis posterior. In this case degeneration was seen in the middle and anterior parts of gyrus suprasylvius leaving gyrus suprasylvius posterior completely free of degeneration.

The other cases fall in between these two extremes. Thus the lesion in KPu 18 was somewhat more oral than in KPu 16, but caudal to the lesion in KPu 17 and the resulting area of degeneration was slightly oral to that in KPu 16. Unfortunately a detailed picture of the topographical arrangement of the projection of the pulvinar to the gyrus suprasylvius cannot be obtained from this material. The reason for this is that the exact boundaries of the pulvinar's projection were obscured by degeneration from the electrode tract being superimposed on degeneration from the pulvinar.

Our findings concerning the topographical organisation of the pulvino-suprasylvian projection do not corroborate those of Waller and Barris (1937). Their results suggest that the ventral part of the pulvinar projects to a more anterior part of gyrus suprasylvius than the dorsal part. The distribution of our lesions within the pulvinar does not allow a dorso-ventral organisation of the pulvinar to be ascertained from our

material. Further, the assumption of such an organisation was based on only two cases in the series of Waller and Barris (1937).

We therefore conclude that the pulvinar has a large projection to area 19 (visual area III of Hubel and Wiesel, 1965) and that this projection is topographically organised in so far as the caudal end of the pulvinar projects to the caudal part of area 19 and the oral part to the anterior end of area 19.

The projection area of nucleus lateralis posterior lies anterior to the projection area of the pulvinar.

(ii) The Auditory Area

The position of the cortical auditory area in the cat has been investigated neuro-physiologically and neuroanatomically (Kornmüller, 1933; Rose and Woolsey, 1949).

The auditory area recognised by Kornmüller (1933) and Bremer and Dow (1939) corresponds to the auditory area AI of Rose and Woolsey (1949). This is the primary auditory area which lies in the dorsal part of the anterior and middle ectosylvian gyri and is cytoarchitectonically distinct from the surrounding cortex (Bremer and

Dow, 1939).

Ventral to area AI lies the second auditory area AII, and a third auditory area named Ep has been recognised in the posterior ectosylvian gyrus (Rose and Woolsey, 1949). The position and extent of these additional auditory areas was determined electrophysiologically by stimulation of the cochlear nerve. Anatomically they cannot be localised with the commonly used method of retrograde degeneration, as ablation of neither area AII, nor area Ep, leads to retrograde degeneration of the medial geniculate body, as is the case after ablation of area AI. However, if all three areas (AI, AII and Ep) are ablated, the resulting area of retrograde degeneration in the medial geniculate body is far larger than if the lesion were restricted to area AI (Diamond, Chow and Neff, 1958). The reason for this is that area AI receives an essential type of projection, while area AII and Ep receive a sustaining type of projection (Rose and Woolsey, 1949). These two types of thalamo-cortical projection were first described by Rose and Woolsey (1949), who postulated that axons of thalamic nuclei projecting to specific cortical areas also gave off collateral fibres to the adjacent cortex. Ablation of the specific cortical area would therefore not cause total degeneration of the nucleus because of sparing of some of the collateral fibres.

A lesion of the adjacent cortex would result in degeneration of collateral fibres only, with little effect on the nucleus. Total degeneration of the nucleus will only occur if all axons and their collaterals are destroyed. This explains why the larger area of degeneration is followed by ablation of the three auditory areas (AI, AII and Ep). For the same reason it is difficult to determine the exact position of the ventral boundary of areas AII and Ep. According to Waller (1940) they extend ventrally as far as the upper tip of the sylvian sulcus.

In all our cases, with the exception of KPu 29, a dense island of degeneration was seen in the antero-ventral corner of the middle ectosylvian gyrus. The size of this island was very constant. Its position varied very slightly from one case to another. In some cases it was completely within the limits of area AII as defined by Waller (1940) while in other cases a quarter to a third of the island was ventral to area AII.

We regard these minor differences as being due to individual variation. From the results we conclude that the pulvinar projects to the anterior-ventral part of the gyrus ectosylvius medius, which is part of

the second auditory area AII. This confirms the assumption of Diamond and Neff (1957) that one of the secondary auditory areas receives a projection from the pulvinar, because they found no retrograde degeneration in the pulvinar after ablating area AI but degeneration was present in the pulvinar after lesions involving all three auditory areas.

Single degenerated fibres scattered throughout the middle and posterior ectosylvian gyri are not regarded as significant.

(iii) The Limbic Area

With the exception of case KPu 29, in which the lesion was small and posteriorly placed, all cases showed degeneration in the parasplenial gyrus.

We think it unlikely that this degeneration is derived from the pulvinar. No such projection was demonstrated by Waller and Barris (1937) in their investigation of the thalamo-cortical projection in the cat, nor has such a projection been demonstrated in the monkey (Walker, 1935; Le Gros Clark and Northfield, 1937; Walker, 1938a and 1938b; Chow, 1950; Simpson, 1952; Bucy and Klüver, 1955; Locke, 1960).

On the other hand, Locke, Angevine and Yakovlev

(1964) have shown that the nucleus lateralis dorsalis projects to the parasplenial gyrus. The posterior end of nucleus lateralis dorsalis lies medial to nucleus lateralis posterior and dorsal to nucleus mediodorsalis and merges with the oral pulvinar (Locke, Angevine and Yakovlev, 1964). This nucleus was affected in most of our cases and it is significant that in case KPu 17 with the most anteriorly placed lesion, involving nucleus lateralis dorsalis, the largest number of degenerated fibres were seen in the parasplenial gyrus.

We therefore conclude that the degeneration seen in the parasplenial gyrus is derived from the nucleus lateralis dorsalis, the posterior end of which had been affected by our lesion. Our findings thus confirm those of Locke, Angevine and Yakovlev (1964), obtained by the method of retrograde degeneration, namely that the pulvinar has no projection to the parasplenial gyrus.

(iv) Other Cortical Areas

The only other cortical area in which degenerated fibres were observed was the suprasplenial gyrus. Scattered single degenerated fibres were seen in this gyrus in all cases including the control KPu 28.

The small number of degenerated fibres seen in this

gyrus, as well as the presence of degeneration in this gyrus in a control case in which the lesion involved part of the thalamic radiation, has caused us not to regard this finding as very significant.

We think that a projection from the pulvinar to this gyrus is highly unlikely, but with our present knowledge, the existence of such a projection cannot be positively excluded.

CHAPTER V

THE CORTICO-PULVINAR PROJECTION

V.1 GENERAL

(a) The Cortico-pulvinar Projection in the Cat

(i) The Visual Area

A connection between the visual cortex and the pulvinar was demonstrated for the first time by Sachs (1909). In his experiments the lesion which caused degeneration in the pulvinar involved the lateral and suprasylvian gyrus, thus affecting areas 17, 18 and 19.

By using the method of physiological neuronography of de Barenne and McCulloch (1938), Niemer and Jiménez-Castellanos (1950) were able to confirm the findings of Sachs. Responses were recorded in the pulvinar after strychninization of both the medial surface of the lateral gyrus (area 17), and the lateral surface of the lateral gyrus (area 18). The strongest responses in the pulvinar were recorded after strychninization of what is termed association cortex by Niemer and Jiménez-

Castellanos (1950), but by being the posterior part of the suprasylvian gyrus, is in fact area 19.

After lesions in the lateral gyrus affecting areas 17 and 18, Altman (1962) found numerous degenerated fibres present in the pulvinar and nucleus posterior. The abundance of degenerated fibres in these two nuclei contrasted sharply with the near absence of degenerated fibres in the lateral geniculate body.

According to Majorossy, Réthelyi and Szentágothai (1965) the cortico-pulvinar fibres are mainly derived from the secondary visual areas (18 and 19) and only to a much lesser extent from the primary visual area (area 17).

In an extensive investigation on the projection of the striate and extrastriate cortex, Garey, Jones and Powell (1968) found a projection to the pulvinar only from area 19. Unlike Altman (1962) they found a large projection from the visual cortex to the lateral geniculate body.

There is general agreement therefore on the presence of a projection from the visual cortex to

the pulvinar among these investigators. This projection appears to be mainly from area 19 and to a much lesser degree from areas 17 and 18.

(ii) The Auditory Area

Sachs (1909) described degeneration in the pulvinar after a lesion of 10mm by 10mm involving both the middle and the posterior ectosylvian gyri.

This finding was confirmed by Niemer and Jiménez-Castellanos (1950) by physiological neuronography. Unfortunately the strychninization also involved both the middle and posterior ectosylvian gyri in their case with the result that we know that a connection exists between the secondary auditory cortex and the pulvinar, but whether this projection arises from both secondary auditory areas, namely AII and Ep, or whether only one is involved is not known.

(iii) Other Cortical Areas

From the work of Niemer and Jiménez-Castellanos (1950) it appears that the association cortex anterior to the visual cortex in the lateral and suprasylvian gyri projects to the pulvinar. This can be looked upon as the parietal association

cortex of the cat.

(b) The Cortico-pulvinar Projection in the Primate

It is essential to point out that although we have attempted to compare the findings in subprimates, and primates, with those in man, this is not always possible.

The greatest problem in this connection is presented by the cortex at the junction of the parietal, occipital and temporal lobes. This cortex undergoes the greatest elaboration in phylogeny and this leads to the formation of the angular and supramarginal gyri in man (Walker, 1938). These gyri, or the equivalent cytoarchitectural cortical areas (areas 37, 39 and 40), are absent in Macaca mulatta.

The constituents of the occipital lobe in the Macaca mulatta are very different from the constituents of the occipital lobe in man. Thus the greater part of the occipital lobe of the Macaca mulatta (approximately 95%) is area 17, there being only a very narrow strip of area 18 between area 17 and the simian sulcus. The greater part of area 18 and all of area 19 lie in the parietal lobe. In man, area 17 is limited to a relatively small area along the calcarine fissure and areas 18 and 19 are completely within the occipital lobe (Polyak, 1955).

As far as the temporal lobe is concerned, there is much similarity between monkey and man. In both all three temporal gyri can be recognised, with the superior temporal gyrus being area 22, the middle gyrus area 21, and the inferior gyrus area 20. It must however be remembered that a considerable part of the tip of the temporal lobe in man constitutes area 38, while in the monkey the areas 22 and 21 continue as far as the tip and in the case of area 21, onto the medial surface of the temporal lobe (Brodman, 1909).

In the following paragraphs the term visual area will be used to mean areas 17, 18 and 19, but will not be synonymous with occipital lobe, as areas 18 and 19 extend into the parietal lobe in the monkey.

The term auditory area will be used for the three temporal gyri, or areas 22, 21 and 20, as well as the primary auditory areas 41 and 42. The extent to which these areas are comparable with the auditory areas A1, A11 and Ep of the cat is not clear. We know that the auditory radiation projects mainly to area 41, but it also projects to area 42 (Truex and Carpenter, 1969). Area 22 is known to receive fibres from areas 41 and 42, and project to the parietal, occipital and insular cortex (Bailey, von Bonin, Garol and McCulloch, 1943).

Lesions of area 22 on the dominant hemisphere, or bilateral lesions, cause word deafness. If the lesion is more posteriorly situated, auditory agnosia occurs (Truex and Carpenter, 1969). The superior temporal gyrus (or area 22) is therefore clearly connected in some way with auditory function. Little is known about the function of the middle and inferior temporal gyri.

(i) The Visual Area

The possibility of a projection from the visual cortex to the pulvinar has not been studied neuroanatomically in the primate.

To the best of our knowledge, this projection in the primate has only been studied with the method of physiological neuronography of de Barenne and McCulloch (1938), by Jasper, Marsan and Stoll (1952). These authors came to the following conclusion.

"These results suggest that the preferential pathways of conduction from the visual receiving area of the cortex are not directly to other areas of the cortex, but back to subcortical structures in the thalamus and midbrain." The major projection to the pulvinar and the lateral geniculate nucleus was derived from area 17. The impulse was conducted along this route in preference to being conducted to

the adjoining area 18. Area 19 was also found to project to the pulvinar, but not to the lateral geniculate nucleus. Again impulses travelled more readily to the pulvinar than to the adjacent cortex.

In view of the absence of any anatomical investigation on the existence of a projection from the visual cortex to the pulvinar, the investigation in this chapter will be completely devoted to this problem.

(ii) The Auditory Area (temporal lobe)

It has been known for some time that there exists a large projection from the temporal lobe to the pulvinar (Papez, 1937; Rundles and Papez, 1938; Papez, 1939; Bucy and Klüver, 1955).

Although there was little doubt about the presence of a temporo-pulvinar projection, its exact origin was rather obscure, because these observations were based on cases with large lesions, or even temporal lobectomies.

Fortunately the work of Jasper, Marsan and Stoll (1952) and Whitlock and Nauta (1956) provide much more information on the origin of this projection.

The superior temporal gyrus consists of the area TA of von Bonin and Bailey (1947) or the area 22 of Brodmann (1909). This area was found to project to the ventral and caudomedial regions of pulvinar by both Jasper, Marsan and Stoll (1952), using the method of physiological neuronography, and Whitlock and Nauta (1956) using the Nauta-Gygax method. Both groups of investigators also found a projection from this area to the medial geniculate body. The primary auditory cortex lies on the dorsal surface of the superior temporal gyrus, within the sylvian sulcus. It consists of areas TB and TC of von Bonin and Bailey (1947), or areas 41 and 42 according to the classification of Brodmann (1909). The primary auditory cortex projects to the adjacent area 22 (Truex and Carpenter, 1969) and back to the medial geniculate body, which in turn is also the only afferent subcortical connection of the primary auditory cortex.

The anterior temporal region is the area TG of von Bonin and Bailey (1947), and consists of the anterior end of areas 20, 21 and 22 of the classification of Brodmann (1909). Many fibres from this area were found to terminate in the medial pulvinar by both Jasper et al. (1952) and Whitlock and Nauta (1956).

The middle temporal gyrus consists of the dorsal part of field TE of von Bonin and Bailey (1947) or the greater part of area 21 according to the classification of Brodmann (1909). Fibres from this area were found to terminate in the central part of the pulvinar, the pretectal area and superior colliculus by Whitlock and Nauta (1956).

The inferior temporal gyrus consists of the ventral part of field TE of von Bonin and Bailey (1947) or the greater part of area 20 of Brodmann (1909). Less than half of the fibres from this area project to the thalamus. They terminate in the dorsal part of the pulvinar and nucleus lateralis posterior. No fibres continue to pretectum or tectum (Whitlock and Nauta, 1956).

Stimulation of an area which in our opinion involves the posterior part of area 20 as well as a part of area 19 of Brodmann (1909), produced after discharges in the lateral and adjacent part of the medial pulvinar, and in the medial geniculate body (Jasper et al., 1952).

The differences between the findings of Jasper et al. (1952) and Whitlock and Nauta (1956)

are not necessarily contradictory as the electrophysiological technique of Jasper et al. (1956), in contrast to degeneration studies can demonstrate functional connections involving more than one synapse.

(iii) Other Cortical Areas

Various investigators who have studied the efferent projection from the remaining extent of the parietal cortex, and the frontal cortex, have found no sign of a projection to the pulvinar from these areas (Krieg, 1954; Kuwana and Kusama, 1964; De Vito and Smith, 1964; Chandler, 1964; Campos-Ortega and Cluver, 1969).

V.2 MATERIAL AND METHODS

Eleven normal young adult Macaca mulatta with bodyweights ranging from 6.5 Kg to 8.5 Kg were used for this investigation. The post-operative survival time of the individual animals is given in table V.1.

(a) Anaesthesia

Fluothane was used in an open drip for both induction and maintenance of anaesthesia. In this way the level of anaesthesia could be controlled very easily.

(b) Operation

A craniectomy was performed in the occipital area. After incising the dura mater a subpial aspiration was performed using a fine glass canula attached to a vacuum line. Great care was taken to avoid damage to the underlying white substance. With the aid of a Zeiss operating microscope, aspiration could be kept to a very shallow level and damage to blood vessels could be avoided. In these animals the dura was thick enough to allow suturing.

(c) Perfusion

After a post-operative survival period of 6 to 15 days (table V.1) the animals were perfused with 10% formal saline. The same procedure was followed as was described in Chapter III for the pig.

(d) Sectioning and Staining

Before sectioning the brains were placed in a 30% sucrose solution for two days to prevent the formation of crystals. As in the previous cases four parallel series of frozen sections were made and stained with the Glees (1946), Nauta and Gygax (1954), Fink and Heimer (1967), and cresyl violet methods, respectively.

T A B L E V.1

CASE	TYPE OF INVESTIGATION	SURVIVAL PERIOD IN DAYS
Mm Vc 1	Electron	2
Mm Vc 2	Microscopical	2
Mm Vc 3		3
Mm Vc 4	Light	Control
Mm Vc 5	Microscopical	13
Mm Vc 6		15
Mm Vc 7		13
Mm Vc 8 & 9	Electron	4 & 11
Mm Vc 10 & 11	Microscopical	5 & 24
Mm Vc 12 & 13		6 & 9
Mm Vc 14 & 15		7 & 150
Mm Vc 16	Light	4
Mm Vc 17	Microscopical	6
Mm Vc 18		6
Mm Vc 19		7
Mm Vc 20		7
Mm Vc 21		11
Mm Vc 22		11
Mm Vc 23 & 24	Electron Microscopical	48

V.3 RESULTS

(a) Macaca mulatta Mm Vc 5

(i) The Lesion

In this case the lesion was situated in the dorsal part of the left occipital operculum and confined to area 17. Included in figure V.1 is a small drawing of the left hemisphere of the brain showing the lesion in solid black. The animal survived for 13 days post-operatively and the brain was sectioned parasagittally.

(ii) The Projection to the Pulvinar

The cortico-pulvinar fibres were seen leaving the cortico-tectal tract grouped together in large bundles. The bundles of degenerated fibres terminated in clusters in the inferior nucleus of the pulvinar (fig. V.1). No sign of retrograde degeneration was seen in the Nissl sections of the pulvinar.

(iii) The Projection to the Lateral Geniculate Body

In the Nissl sections an area of retrograde degeneration was seen in the lateral geniculate body. The outline of the area involved is shown

in figure V.1. In the Nauta and Fink-Heimer sections degenerated fibres were seen, mostly but not exclusively, confined to the area of retrograde degeneration. The degenerated fibres in the Nauta sections were large and had the appearance of degeneration"en passage"and not that of typical preterminal degeneration. In the Fink-Heimer sections there was a dust-like precipitate of silver. Numerous degenerated fibres with the typical drop-like appearance of terminally degenerated fibres were seen in the pregeniculate nucleus. In Glees stained sections, no degenerated boutons were seen. Dark "blotches" with the appearance of silver impregnated neurons were occasionally seen in the Nauta and Fink-Heimer sections, in the same areas in which retrograde degeneration was present in cresyl violet sections (fig. V.3).

(iv) The Projection to the Tectal Area

Fibres to the tectum ran along the tractus cortico-tectalis and terminated in the pretectum and tectum. Those to the pretectum terminated in the nucleus praetectalis and nucleus limitans, while the fibres continuing to the tectum, terminated in the stratum zonale, griseum superficiale

Fig. V.1

The diagram shows sagittal sections of the lateral geniculate body and pulvinar of case Mm Vc 5.

Abbreviations: PL: lateral pulvinar; PI: inferior pulvinar; pg: pregeniculate nucleus; rt: reticular nucleus of thalamus; tct: cortico-tectal tract.

and stratum opticum of the superior colliculus. A few fibres also terminated in the griseum intermedius.

(v) The Projection to other Sub-cortical Areas

Fibres terminated in the caudal part of the body of the caudate nucleus, the zona incerta, the dorsolateral part of the griseum pontis, and the nucleus reticularis thalami.

(b) Macaca mulatta Mm Vc 6

(i) The Lesion

Most of the dorsolateral surface of the occipital lobe and therefore the greater part of area 17 was involved. In addition the lesion also extended onto the parietal lobe, thus affecting most of areas 18 and 19 (fig. V.2). The animal survived for 15 days post-operatively.

(ii) The Projection to the Pulvinar

In the pulvinar three areas of termination could be distinguished. As in the previous case, a large number of fibre bundles terminated in the inferior pulvinar. Additionally a large number of degenerated fibres were seen in the lateral

part of the lateral pulvinar and occasional single degenerated fibres occurred in the lateral border of the medial pulvinar (fig. V.2).

There were no signs of retrograde degeneration in the Nissl sections and no argyrophilic "blotches" were seen in the sections impregnated according to the Nauta or Fink-Heimer methods.

(iii) The Projection to the Lateral Geniculate Body

A large area of retrograde cellular degeneration was seen in Nissl sections of this nucleus. The area of retrograde degeneration in the lateral geniculate is shown in figure V.4. Degenerated fibres were seen in this nucleus in Nauta sections, but the fibres were thick and had the appearance of degeneration"en passage". Degenerated boutons were not apparent in Glees sections and the Fink-Heimer sections showed some dust-like particles, but without concomitant preterminal fibre degeneration. The large fragmented fibres were seen throughout the nucleus and not only in the area of retrograde degeneration. In the area of retrograde degeneration occasional argyrophilic "blotches" resembling neurons, were seen (fig. V.3). In the nucleus praegeniculatus numerous bundles of degenerated

Fig. V.2

Coronal sections of the thalamus case Mm Vc 6.

Abbreviations:

ca: caudate nucleus;
cgl: lateral geniculate body;
cgm: medial geniculate body;
CM: centrum medianum;
GP: griseum pontis;
Ld: lateralis dorsalis;
LP: lateralis posterior;
md: medio dorsalis;
PI: pulvinar inferior;
PL: pulvinar lateralis;
PM: pulvinar medialis;
PO: pulvinar oralis;
prt: praetectal nucleus;
pu: putamen;
pf: parafascicularis;
ru: nucleus rubor;
sn: substantia nigra;
VL: ventralis lateralis;
VPLc: ventralis postero-lateralis pars caudalis;
VPM: ventralis postero-medialis;
Zi: zona incerta.

Fig. V.3

This figure consists of four photomicrographs of the lateral geniculate body of case Mm Vc 6.

Large dark argyrophilic "blotches" resembling neurons can be seen in each photomicrograph.

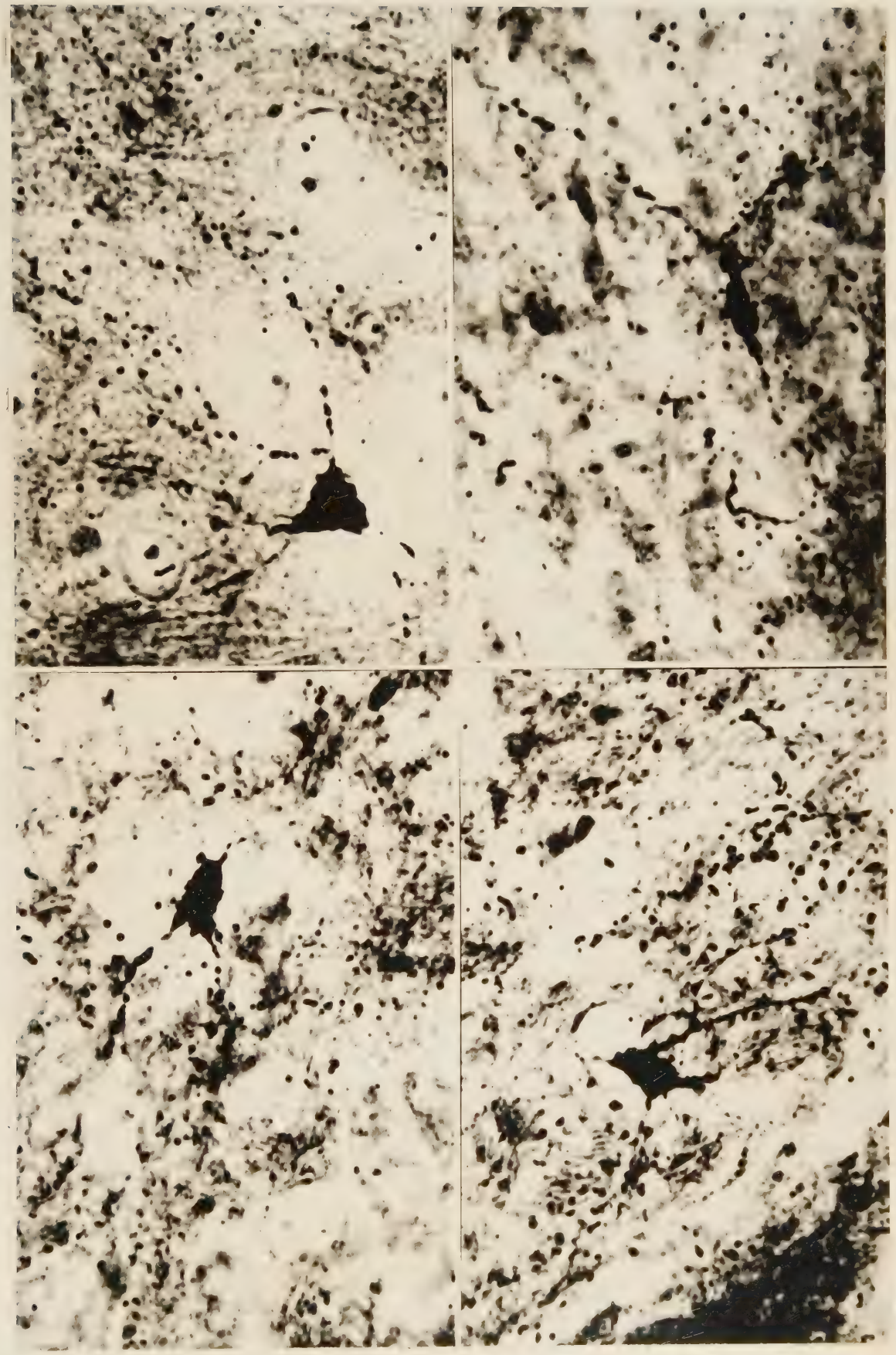


Fig. V. 3.

fibres terminated. These bundles consisted of highly fragmented fibres showing typical drop-like degeneration.

(iv) The Projection to the Tectal Area

The fibres ran along the cortico-tectal tract and terminated in the nucleus limitans and nucleus praetectalis of the pretectum and the superficial three layers of the tectum.

(v) The Projection to other Sub-cortical Areas

Terminal degeneration was seen in the body of the caudate nucleus and dorsal and caudal parts of the putamen. A bundle of fibres traversed the optic radiation and entered the zona incerta. A few of these fibres terminated in the zona incerta while the remainder continued to terminate in the nucleus suprapeduncularis, tegmentum praerubricum and finally in the pars parvocellularis of the red nucleus. Terminal degeneration was also seen in the laterodorsal part of the griseum pontis and the nucleus lateralis dorsalis.

(c) Macaca mulatta Mm Vc 7

(i) The Lesion

In this case the lesion was restricted to the

peri- and para-striate cortex or areas 18 and 19. As can be seen in figure V.5, the lesion was restricted to two separate areas; dorsally it affected the gyri occipitalis and parietalis superior, while ventrally it affected the cortex on either side of the inferior occipital sulcus. This rather extraordinary lesion was the result of a fortunate accident. We had attempted to ablate the superior occipital and parietal gyri only, but after perfusion a bloodclot was discovered on the ventral surface of the occipital lobe. The lesion described above, which was histologically verified, was apparently the result of pressure from the clot.

(ii) The Projection to the Pulvinar

A large number of terminally degenerated fibres were seen in the inferior and lateral parts of the pulvinar.

(iii) The Projection to the Lateral Geniculate Body

No terminally degenerated fibres or degeneration en passage was seen in the lateral geniculate body. A large number of terminally degenerated fibres were seen in the nucleus praegeniculatus.

(iv) The Projection to the Tectal Area

Degenerated fibres terminated in the pretectum

Fig. V.4

The diagram shows serial coronal sections of the lateral geniculate body of case Mm Vc 6.

Areas where retrograde degeneration occurred are shown in solid black. Large degenerated fibre bundles are shown as large black dots.

Terminal degeneration, seen only in the pregeniculate nucleus and inferior pulvinar, is shown as fine dots.

Fig. V 4

Serial coronal sections of the lateral geniculate body of case Mm Vc 6.

Fig. V.5

The diagram shows serial sagittal sections of the visual cortex and posterior thalamus of case Mm Vc 7.

Abbreviations: Ca: caudate nucleus; GL: lateral geniculate body; GM: medial geniculate body; GP: griseum pontis; ntoa: nucleus tractus opticus accessorius; PI: pulvinar inferior; PL: pulvinar lateralis; Prt: pretectal nucleus; rt: reticular nucleus; SO: stratum opticum.

in the nucleus limitans and nucleus praetectalis. In the tectum terminal degeneration was seen in the stratum zonale, griseum superficiale and stratum opticum.

(v) The Projection to other Sub-cortical Areas

A few degenerated fibres terminated in the zona incerta, dorsolateral part of the griseum pontis, the nucleus reticularis thalami and nucleus lateralis dorsalis.

(d) Macaca mulatta Mm Vc 17

(i) The Lesion

The lesion was made in the orodorsal part of the left occipital operculum, and therefore completely confined to area 17 (fig. V.6 and V.7).

(ii) The Projection to the Pulvinar

The cortical fibres reached the pulvinar along two different pathways (fig. V.6). One pathway approached the ventral side of the pulvinar with the temporo-thalamic fasciculus of Arnold and the other the dorsolateral side with the cortico-tectal fibres. The ventrally approaching fibres terminated in clusters in the inferior pulvinar. The areas

of terminal degeneration were restricted to the dorsal half of the inferior pulvinar. Fibres leaving the cortico-tectal tract terminated in the lateral pulvinar in a thin band along its dorso-lateral border, immediately next to the external medullary lamina.

(iii) The Projection to the Lateral Geniculate Body

There were no signs of retrograde degeneration in the Nissl sections. In the Nauta sections large degenerated fibres, restricted to a wedge-shaped area in the middle of the lateral geniculate body were seen. Neither these fibres nor those seen in Fink-Heimer and Glees sections, had the typical appearance of terminal degeneration. In Fink-Heimer sections, argyrophilic "blotches" with the appearance of neurons were seen. These cells were distributed throughout a wedge-shaped area in the middle of the lateral geniculate body corresponding to a similar area containing large degenerated fibres in Nauta stained sections (fig. V.7).

(iv) The Projection to the Tectal Area

Fibres left the cortico-tectal tract at the pretractal area and terminated in the pretectal nucleus. The remaining fibres continued to the

Fig. V.6

This diagram shows serial coronal sections of the posterior thalamus of case Mm Vc 17.

Abbreviations: ca: nucleus caudatus; GL: lateral geniculate body; GM: medial geniculate body; GP: griseum pontis; nt oa: nucleus tractus opticus accessorius; PI: pulvinar inferior; PL: pulvinar lateralis; Prt: pretectal nucleus; rt: reticular nucleus; SO: stratum opticum.

Fig. V.7

This diagram shows three serial coronal sections of the lateral geniculate body of case Mm Vc 17.

tectum where they terminated in the extreme lateral parts of the stratum zonale, griseum superficiale and stratum opticum.

(v) The Projection to other Sub-cortical Areas

Terminal degeneration was seen in the dorso-lateral part of the griseum pontis and the nucleus tractus opticus accessorius.

(e) Macaca mulatta Mm Vc 18

(i) The Lesion

The lesion occupied the middle of the lateral aspect of the occipital operculum and was therefore completely confined to area 17 (fig. V.8 and V.9).

(ii) The Projection to the Pulvinar

As described in the previous case, degenerated fibres reached the pulvinar along two pathways. The ventrally approaching fibres terminated in the middle of the inferior pulvinar. The area of termination in the inferior pulvinar was much the same as in the previous case except that it extended further orally. Fibres from the cortico-tectal tract again terminated in the lateral part of the lateral pulvinar. It should be noted that the

area of termination was somewhat more ventral than in the previous case (fig. V.8).

(iii) The Projection to the Lateral Geniculate Body

There were no signs of retrograde degeneration in Nissl sections. A band-shaped area containing large degenerated fibres with the appearance of degeneration en passage was present in Nauta stained sections. In Fink-Heimer stained sections argyrophilic "blotches" with the appearance of neurons were seen. This band-shaped area was considerably more laterally situated than in case Mm Vc 17 (fig. V.9).

(iv) The Projection to the Tectal Area

Terminal degeneration was seen in the pretectum in the nucleus limitans and nucleus praetectalis. Fibres to the tectum terminated in the stratum zonale, the griseum superficiale and stratum opticum. In each layer the area of degeneration was confined to the lateral part of the middle third of that layer. The area of degeneration was therefore more medially situated than in case Mm Vc 17.

(v) The Projection to other Subcortical Areas

Terminal degeneration was seen in the dorso-

Fig. V.8 The diagram shows serial coronal sections of the posterior thalamus of case Mm Vc 18.

Abbreviations: ca: caudate nucleus; GL: lateral geniculate body; GM: medial geniculate body; GP: griseum pontis; nt oa: nucleus tractus opticus accessorius; PI: pulvinar inferior; PL: pulvinar lateralis; Prt: praetectal nucleus; sg: stratum griseum superficiale; SO: stratum opticum.

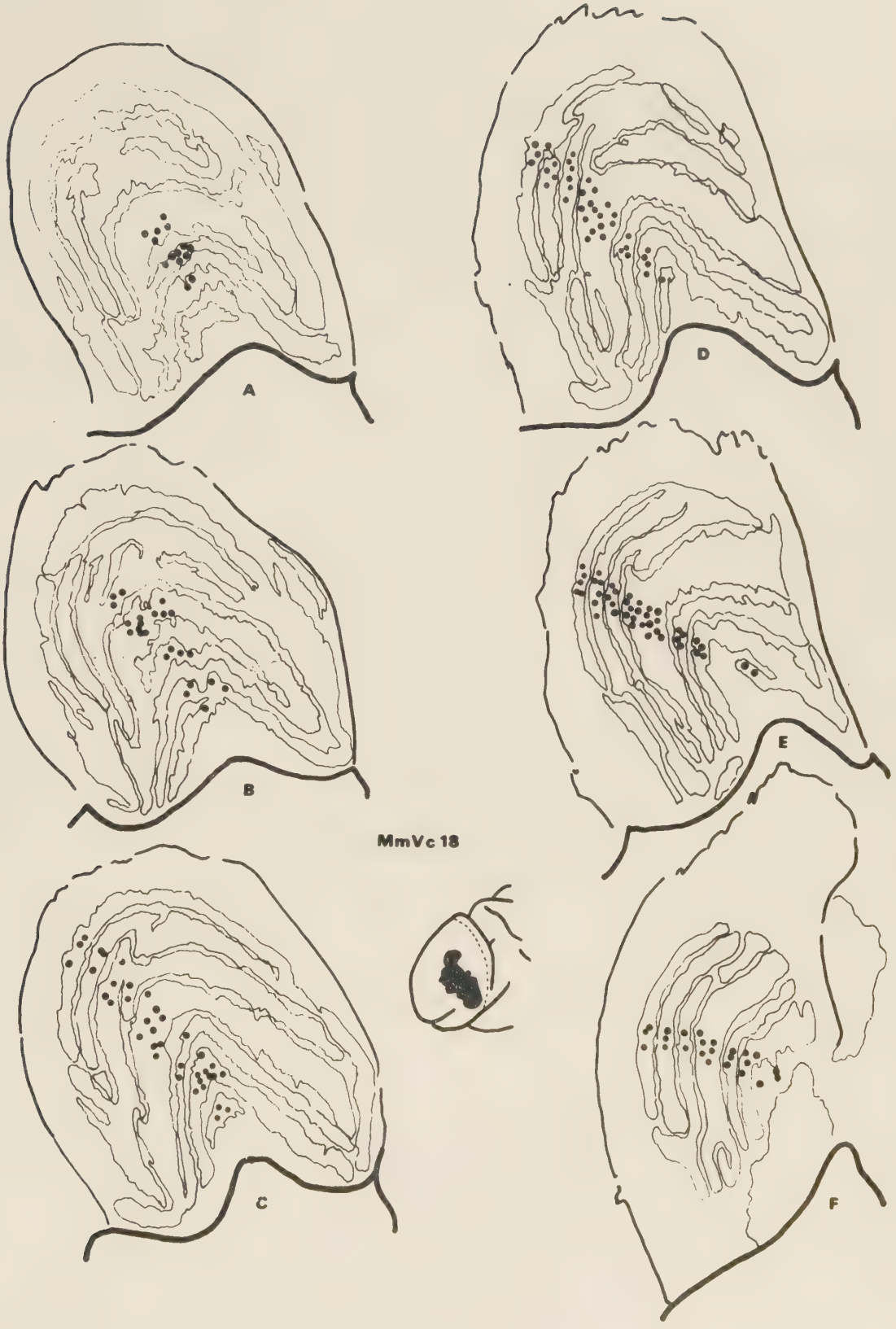


Fig. V.9

The diagram shows serial coronal sections of the lateral geniculate body of case Mm Vc 18.

lateral part of the griseum pontis and the nucleus tractus opticus accessorius.

(f) Macaca mulatta Mm Vc 19

(i) The Lesion

In this case the lesion was more caudally situated than in the previous two cases, and occupied the caudal part of the occipital operculum.

(ii) The Projection to the Pulvinar

Degenerated fibres reached the pulvinar ventrally and dorsolaterally. The former terminated in the inferior pulvinar and the latter in the lateral pulvinar. The distribution of terminally degenerated fibres was much the same as in the inferior pulvinar and somewhat more ventral in the lateral pulvinar (fig. V.10).

(iii) The Projection to the Lateral Geniculate Body

Large degenerated fibres "en passage" as well as silver impregnated neurons were seen in the lateral geniculate body. These fibres and cells were confined to a wedge-shaped area in the middle of the lateral geniculate body (fig. V.11).

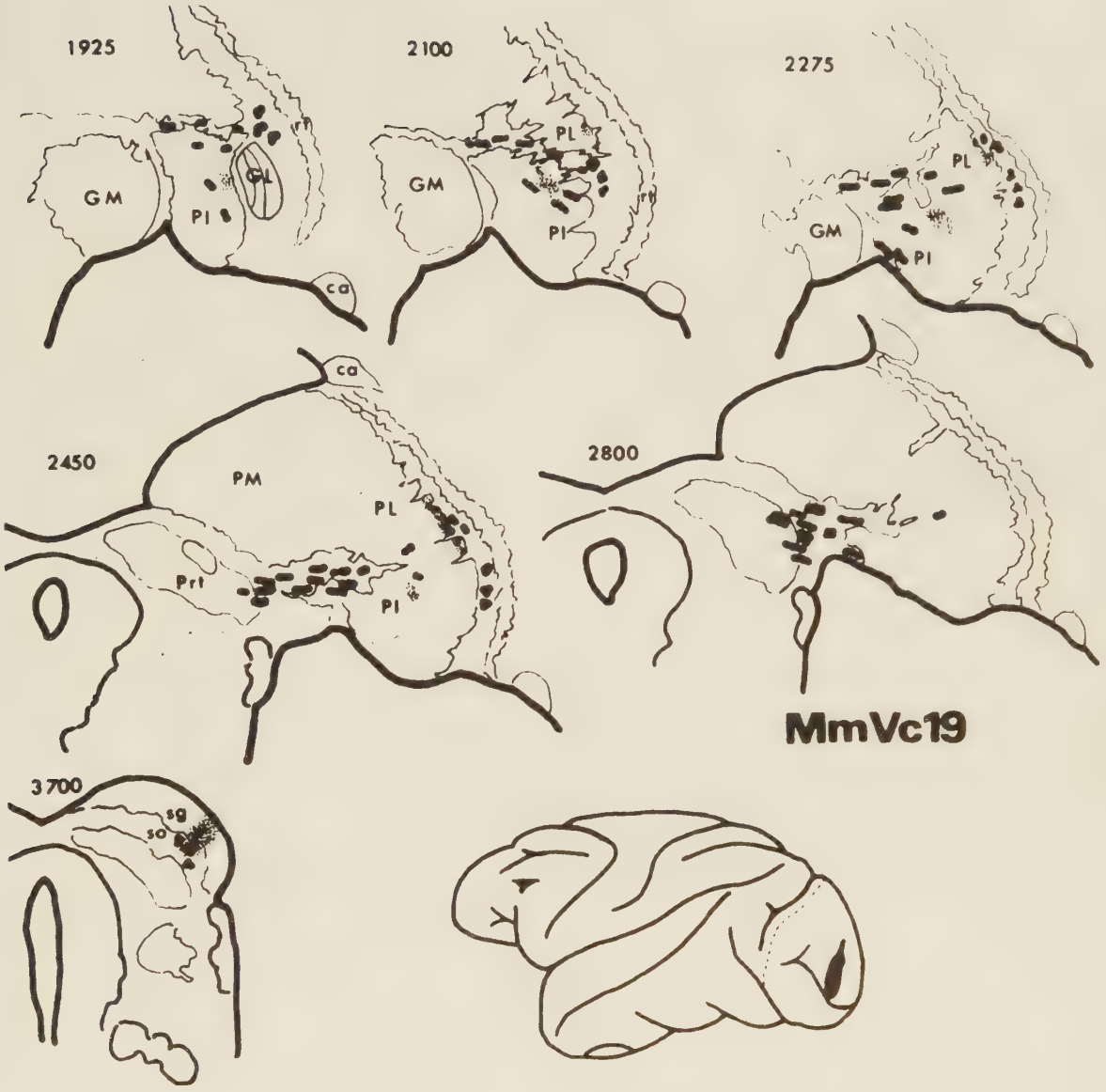


Fig. V.10

The diagram shows serial coronal sections of the pulvinar and tectum of case Mm Vc 19.

Abbreviations: CA: caudate nucleus; GL: lateral geniculate body; GM: medial geniculate body; PI: pulvinar inferior; PL: pulvinar lateralis; PM: pulvinar medialis; Prt: nucleus praetectalis; sg: stratum griseum superficiale; SO: stratum opticum.

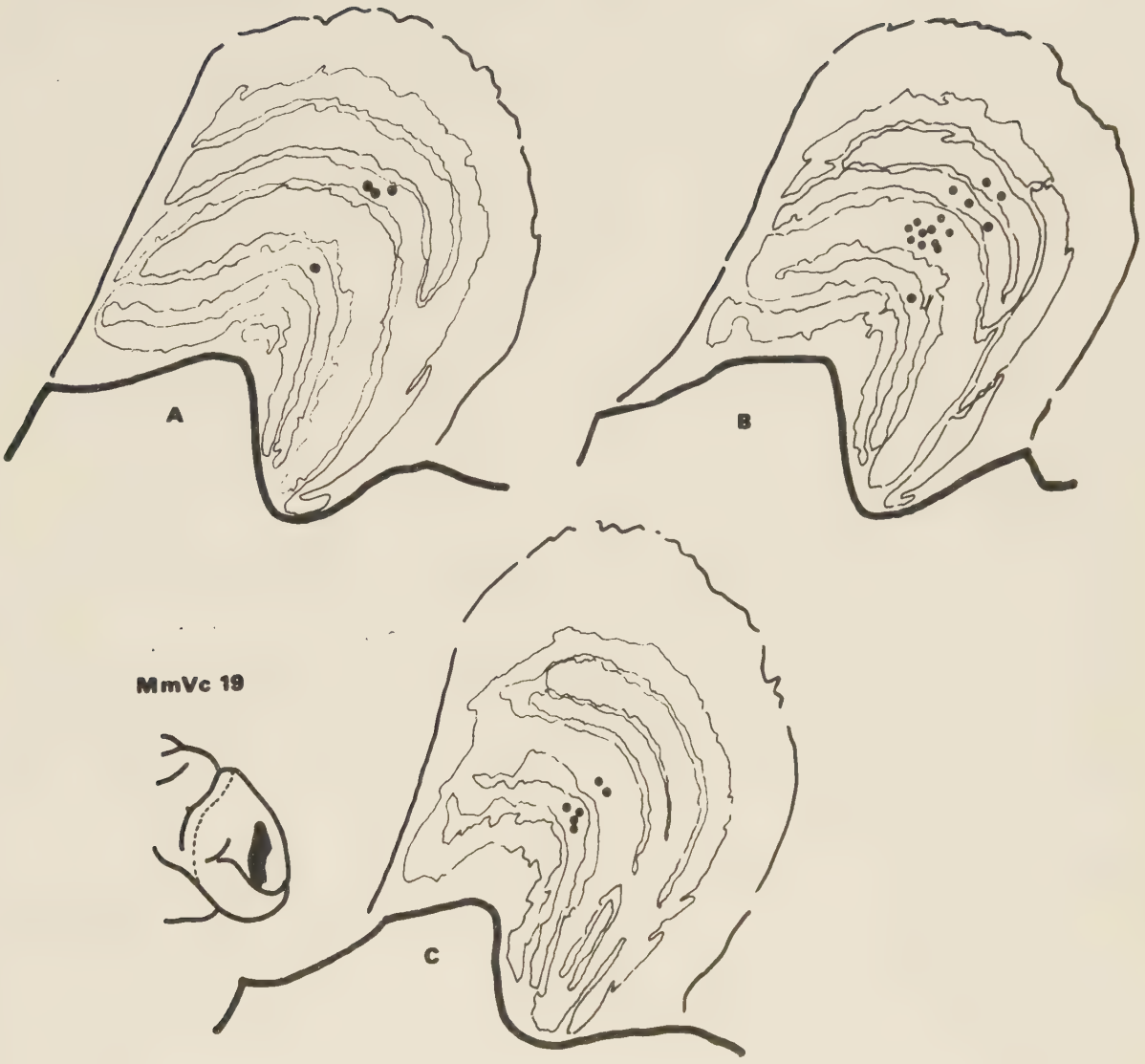


Fig. V.11

The diagram shows three serial coronal sections of the lateral geniculate body of case Mm Vc 19.

(iv) The Projection to the Tectal Area

Fibres from the cortico-tectal tract terminated in the pretectal area in the nucleus limitans and in the nucleus praetectalis. Fibres to the tectum terminated in the stratum zonale, griseum superficiale and stratum opticum. In each layer the area of degeneration was confined to the lateral part of the middle third of that layer.

(v) The Projection to other Sub-cortical Areas

Terminal degeneration was seen in the dorsolateral part of the griseum pontis and the nucleus tractus opticus accessorius.

(g) Macaca mulatta Mm Vc 20

(i) The Lesion

The lesion affected a small part of the oral third of the occipital operculum. The extent of the lesion can be seen in figure V.12 and figure V.13.

(ii) The Projection to the Pulvinar

As in the previous cases the degenerated fibres approached the pulvinar ventrally and dorsolaterally.

The ventrally approaching fibres terminated in the inferior pulvinar. The area of terminal degeneration in the inferior pulvinar was more orally and more dorsally placed than in the previous cases. The area of terminal degeneration in the lateral pulvinar again consisted of a thin band along its lateral border. This area was smaller and more orally situated than in previous cases.

(iii) The Projection to the Lateral Geniculate Body

The lateral geniculate body again only contained large degenerated fibres en passage and numerous silver impregnated neurons. These were distributed throughout a wedge-shaped area in the middle of the lateral geniculate nucleus (fig. V.13).

(iv) The Projection to the Tectal Area

Terminal degeneration was seen in the pretectal area in the nucleus limitans and in the nucleus praetectalis. Fibres to the tectum terminated in the stratum zonale, griseum superficiale and stratum opticum. In each layer the area of degeneration was confined to the middle third of that layer.

(v) The Projection to other Subcortical Areas

Terminal degeneration was seen in the dorso-

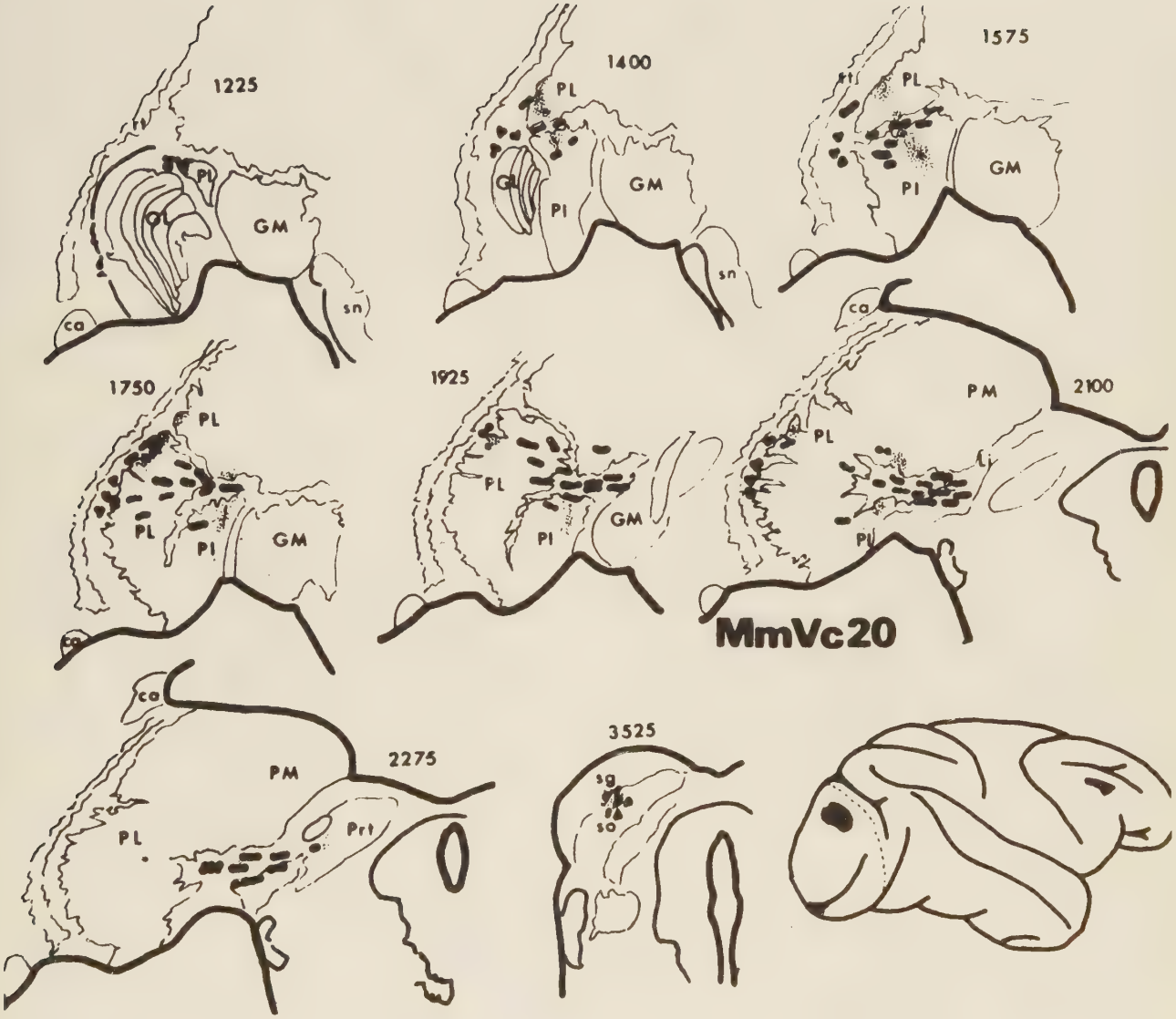


Fig. V.12

The diagram shows serial coronal sections of the pulvinar and tectum of case Mm Vc 20.

Abbreviations: ca: nucleus caudatus; GL: lateral geniculate body; GM: medial geniculate body; PI: pulvinar inferior; PL: pulvinar lateralis; PM: pulvinar medialis; Prt: nucleus praetectalis; rt: reticular nucleus; sg: stratum opticum; sn: substantia nigra.

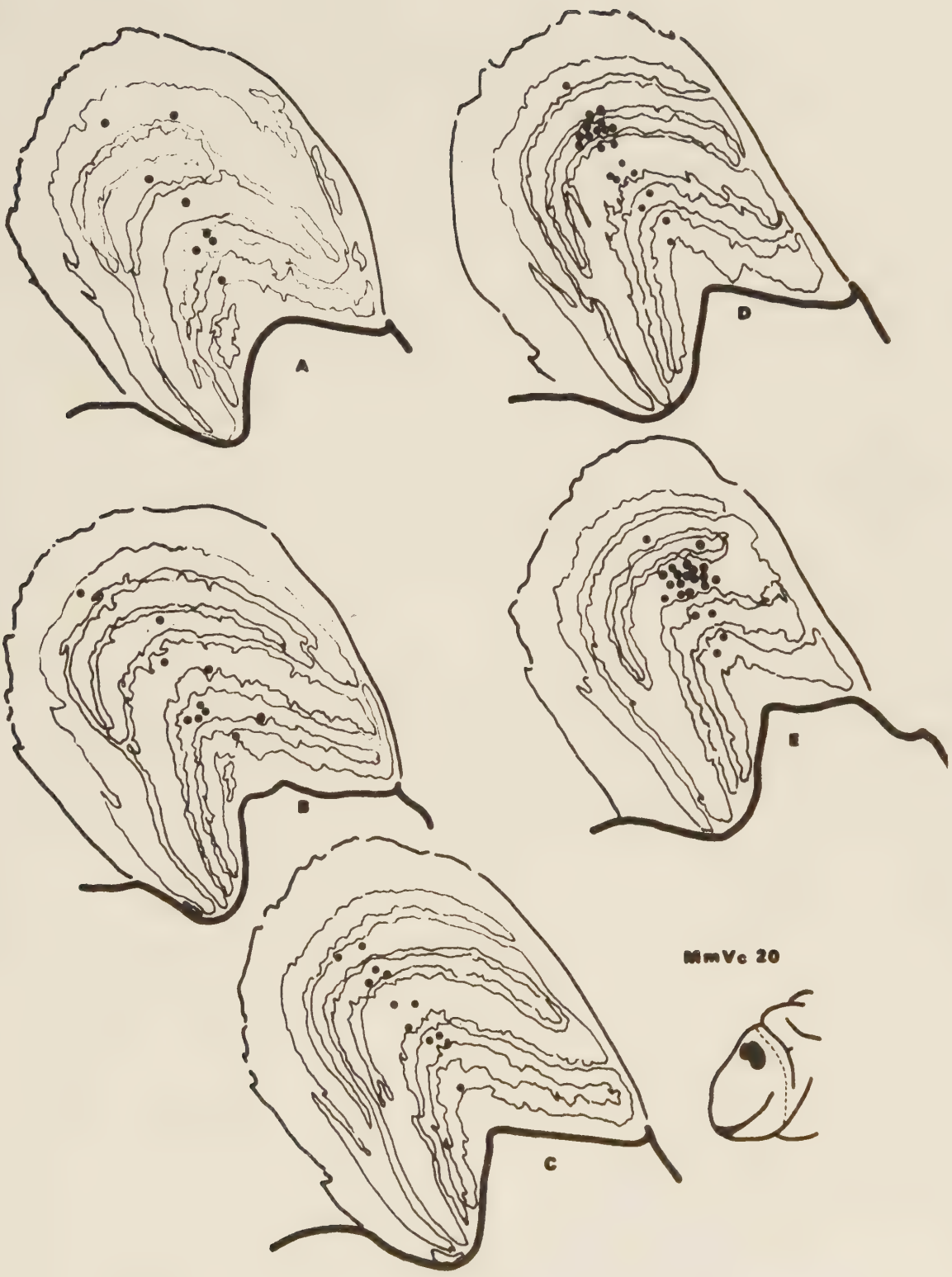


Fig. V.13

The diagram shows serial coronal sections of the lateral geniculate body of case Mm Vc 20.

lateral part of the griseum pontis. A small number of terminally degenerated fibres were seen in the nucleus tractus opticus accessorius.

(h) Macaca mulatta Mm Vc 21

(i) The Lesion

In this case the lesion affected the lower part of area 18 as well as a small strip of area 17 at the boundary of areas 17 and 18, as can be seen in figure V.14.

(ii) The Projection to the Pulvinar

The number of fibres terminating in the inferior pulvinar was considerably less than in the previous cases. Terminal degeneration was confined to the extreme lateral and oral part of the inferior pulvinar. In the lateral pulvinar a larger number of fibres terminated than in the previous cases, in which the lesion was confined to area 17. The terminal degeneration was distributed in the form of a column or band, similar to the previous cases, but situated in the middle of the lateral pulvinar and not along its lateral boundary.

(iii) The Projection to the Lateral Geniculate Body

Degeneration "en passage" and silver impregnated

cells were present in the lateral geniculate body, but only in a single section shown in figure V.15.

(iv) The Projection to the Tectal Area

A small group of fibres ended in the pretectum in nucleus limitans and the nucleus praetectalis. In the tectum fibres ended in the stratum zonale, griseum superficiale and stratum opticum. In each layer the area of degeneration was confined to the lateral third of that layer.

(v) The Projection to other Sub-cortical Centres

A small number of terminally degenerated fibres were seen in the dorsolateral part of the griseum pontis. A few terminally degenerated fibres were present in the nucleus tractus opticus accessorius.

(i) Macaca mulatta Mm Vc 22

(i) The Lesion

In this case it was attempted to destroy the lower lip of the calcarine fissure by approaching it through the occipital operculum. The posterior occipital cortex was pierced with a fine glass canula with which the lower calcarine lip was aspirated. The lesion therefore involved the

Fig. V.14

The diagram shows serial coronal sections of the posterior thalamus and tectal region.

Abbreviations: ca: caudate nucleus; GL: lateral geniculate body; PI: pulvinar inferior; PL: pulvinar lateralis; PM: pulvinar medialis; Prt: nucleus praetectalis; rt: reticular nucleus; sg: stratum griseum superficiale; SO: stratum opticum.

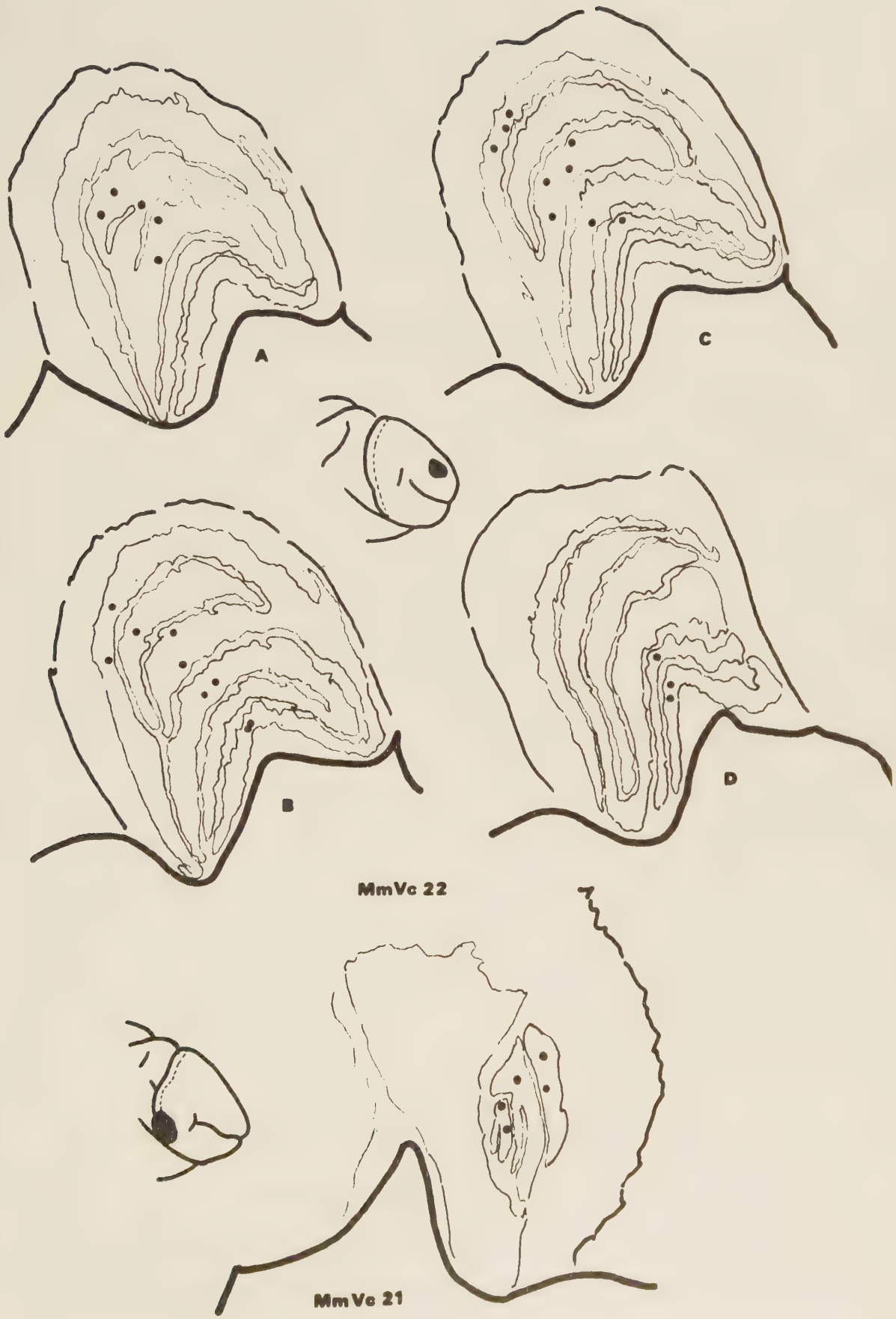


Fig. V.15 The diagram shows serial coronal sections of the lateral geniculate body of case Mm Vc 21.

posterior occipital cortex at the point of entrance, the underlying white matter and part of the lower lip of the calcarine fissure. Notwithstanding the depth of the lesion, only structures related to area 17 were injured.

(ii) The Projection to the Pulvinar

A large number of degenerated fibres reached the inferior pulvinar ventrally, and terminated in the oro-ventral part of this nucleus as can be seen in sections 2450 and 2625 of figure V.16. Fibres from the cortico-tectal tract terminated in the inferior pulvinar in the middle of the caudal part of this nucleus. The two areas of terminal degeneration merged approximately halfway along the antero-posterior extent of the nucleus (section 2800, fig. V.16). Terminal degeneration in the lateral pulvinar was localised in a band along its lateral boundary. This band of degeneration had a greater antero-posterior extent than in the other cases.

(iii) The Projection to the Lateral Geniculate Body

Large degenerated fibres"en passage"and silver impregnated neurons were seen in the lateral geniculate body. These fibres and cells occurred

posterior occipital cortex at the point of entrance, the underlying white matter and part of the lower lip of the calcarine fissure. Notwithstanding the depth of the lesion, only structures related to area 17 were injured.

(ii) The Projection to the Pulvinar

A large number of degenerated fibres reached the inferior pulvinar ventrally, and terminated in the oro-ventral part of this nucleus as can be seen in sections 2450 and 2625 of figure V.16. Fibres from the cortico-tectal tract terminated in the inferior pulvinar in the middle of the caudal part of this nucleus. The two areas of terminal degeneration merged approximately halfway along the antero-posterior extent of the nucleus (section 2800, fig. V.16). Terminal degeneration in the lateral pulvinar was localised in a band along its lateral boundary. This band of degeneration had a greater antero-posterior extent than in the other cases.

(iii) The Projection to the Lateral Geniculate Body

Large degenerated fibres"en passage"and silver impregnated neurons were seen in the lateral geniculate body. These fibres and cells occurred

Fig. V.16

The diagram shows serial coronal sections of the posterior thalamus and tectum of case Mm Vc 22.

Abbreviations: GL: lateral geniculate body; GM: medial geniculate body; PI: inferior pulvinar; PL: lateral pulvinar; PM: medial pulvinar; SG: stratum griseum superficiale; SO: stratum opticum.

in a wedge-shaped area immediately lateral to the middle of the lateral geniculate body.

(iv) The Projection to the Tectal Area

Terminal degeneration was seen in the pretectal area in the nucleus praetectalis and in the nucleus limitans. In the tectum the fibres terminated in the stratum zonale, griseum superficiale and stratum opticum. In each layer the area of degeneration was confined to the middle part of that layer.

(v) The Projection to other Subcortical Areas

Small areas of terminal degeneration were present in the dorsolateral part of the griseum pontis and in the nucleus tractus opticus accessorius.

V.4 DISCUSSION

(a) The Projection to the Pulvinar

The largest efferent projection of the visual cortex is to the pulvinar. While this projection arises mostly, if not exclusively, from the secondary visual cortex in the cat, it is the primary visual cortex from which most

fibres to the pulvinar arise in the primate.

(i) Area 17

Our experiments have shown that there exists a massive projection from area 17 to the inferior pulvinar in the Macaca mulatta. To a much lesser extent area 17 also projects to the lateral pulvinar. The large projection from area 17 to the pulvinar is noteworthy as it has been shown conclusively by Altman (1962) and Garey, Jones and Powell (1968) that area 17 does not project to the pulvinar in the cat. These findings, at first sight, appear to be absolutely contradictory, but this may not be the case.

In Chapter III the nucleus posterior of the cat was considered a possible homologue of the primate inferior pulvinar, because of the findings of Kingston, Vadas and Bishop (1969) of a retinal input to this nucleus.

As far as the efferent projection of the two nuclei is concerned, it has been shown by Chow (1952) that the inferior pulvinar of the Macaca mulatta projects to area 19, and Burrows (1966) and Burrows and Heyhow (1968) have shown that the

nucleus posterior also projects to area 19.

The present work has shown that area 17 projects to the pulvinar in the Macaca mulatta. A projection from area 17 to nucleus posterior of the cat has been described by Altman (1962) and Garey, Jones and Powell (1968).

There thus appears to exist sufficient evidence to regard the inferior pulvinar of the Simian as a homologue of the subprimate nucleus posterior. This would explain the massive area 17 to inferior pulvinar projection found in the Macaca mulatta while a projection from area 17 of the cat to the pulvinar does not exist.

(ii) Area 18

The cortical area 18 of the Macaca mulatta was shown to project to the lateral pulvinar. This is in agreement with the findings of Altman (1962) in the cat. The connection between area 18 and the pulvinar is a reciprocal one as was shown by our experiments on the cat, and the work of Le Gros Clark and Northfield (1937) and Chow (1950) on Macaca mulatta.

(iii) Area 19

We were able to demonstrate a projection from area 19 to the lateral pulvinar. This is in accordance with the findings of Altman (1962) and Garey, Jones and Powell (1968) in the cat. This projection, like that between area 18 and the pulvinar, is also a reciprocal one. A large projection from the pulvinar to area 19 was demonstrated by us in the cat, and such a projection has been described by a number of authors in the primate (Le Gros Clark and NOrthfield, 1937; Walker, 1938b; Chow, 1950). According to Hassler (1965) it was the connection between area 19 and the lateral pulvinar which had degenerated in the case of pure alexia described clinically by Beringer and Stein (1930).

(iv) The Organisation of the Occipito-pulvinar Projection

When the position of the lesion and the position of the resulting degeneration in the pulvinar is compared in each of the cases described, there appears to be a topographical organisation of this projection.

In cases Mm Vc 6, 7 and 21, in which the lesion mainly affected the cortical areas 18 and 19, by far

the greater number of terminally degenerated fibres were found in the lateral pulvinar.

In the cases where the lesions were restricted to area 17, the largest number of terminally degenerated fibres were found in the inferior pulvinar. In all these cases there also existed a thin band of terminal degeneration in the extreme lateral part of the lateral pulvinar. In figure V.17 the position of the lesion as well as the resulting degeneration in the inferior pulvinar is shown for cases Mm Vc 17 to Mm Vc 22. It is apparent that the lesions in the various cases do not overlap and that the degeneration is confined to a particular part of the inferior pulvinar in each case. The organisation of the area 17 - inferior pulvinar projection only becomes apparent however once it is seen as part of the organisation of the visual projection as a whole.

The retino-cortical projection has been studied in great detail by many workers (Polyak, 1932; Talbot and Marshall, 1941; Polyak, 1955; Daniel and Whitteridge, 1961). They found that notwithstanding the magnification which occurs along the course of the projection, (according to Talbot and Marshall (1941) a point at the fovea is enlarged 10,000 times at the visual cortex), there exists a

Fig. V.17

The drawings on the left side of the diagram marked A to E represent serial coronal sections of the inferior pulvinar. In drawing 'A' the lateral pulvinar is also shown. The dots, circles, crosses, etc., delineate the area in which degenerated fibres were found in the different cases. The key to these signs is given in the upper middle part of the diagram.

The drawing on the upper right hand side shows the posterior part of the lateral aspect of a Macaca mulatta brain. The lines numbered 1 to 9 represent the first 9 degrees of the visual field. The work of Talbot and Marshall (1941) was used as a basis for this drawing.

Abbreviations:

HM:	Horizontal meridian
lvm 270:	Lower vertical meridian (270^{o})
uvm 90:	Upper vertical meridian (90^{o})
Scl:	Lateral calcarine sulcus
Sl:	Lunate sulcus
Soi:	Inferior occipital sulcus
Spi:	Inter parietal sulcus
Sta:	Superior temporal sulcus.

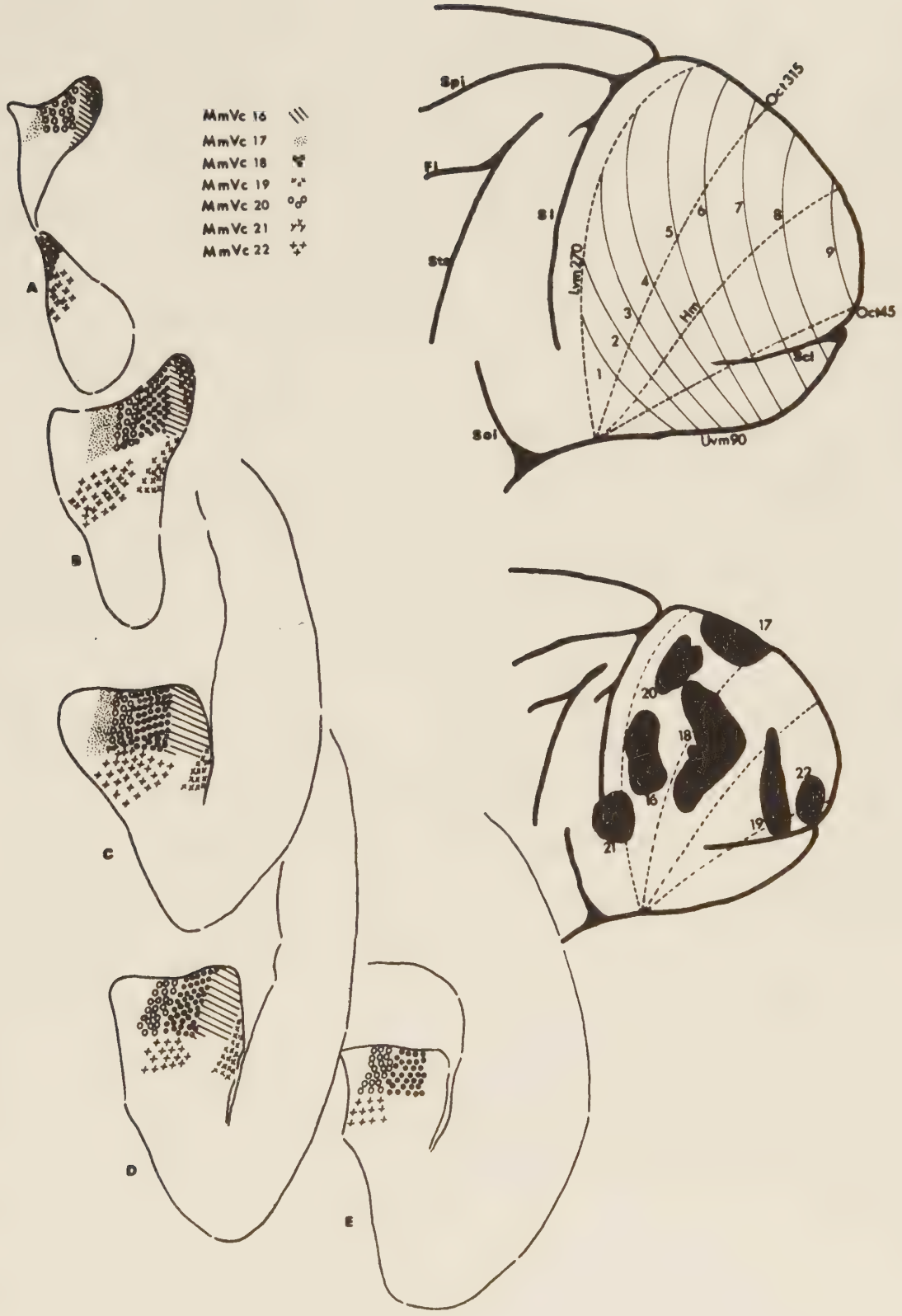

MmVc 16
MmVc 17
MmVc 18
MmVc 19
MmVc 20
MmVc 21
MmVc 22
A
B
C
D
E
Spi
Fl
Str
Bi
Sol
Uvm270
Uvm90
Hm
Scl
Oct315
Oct45
1
2
3
4
5
6
7
8
9
17
20
18
16
21
19
22

Fig. V.17

strict point to point relationship pattern, between retina and cortex. Thus the lower vertical meridan (270^{o}) is represented in the oral limit of the striate area close to the sulcus lunatus; the upper vertical meridian(90^{o}), is represented in the caudo-ventral part of the occipital operculum coinciding with the ventral limit of area 17, close to the inferior occipital sulcus (fig. V.17). Only 9^{o} of the total visual field is represented on the dorso-lateral surface of the occipital lobe. The visual fixation point is therefore localised in the ventro-oral part of the occipital operculum and the representation of the visual hemifield expands radially in a caudo-superior direction. In figure V.17, the cortical lesions and the resulting degeneration in the inferior pulvinar is shown. A comparison between these findings and those of Talbot and Marshall shows that the upper half of the visual hemifield (cases Mm Vc 19 and Mm Vc 22) is represented in the ventral part of the inferior pulvinar whilst the lower half (cases Mm Vc 16, Mm Vc 17, Mm Vc 18, Mm Vc 20, and Mm Vc 21) is represented in the more dorsal part of the inferior pulvinar.

There also appears to exist a latero-medial organisation of the representation of the visual field in the inferior pulvinar. The visual field close to the fovea is presented in the lateral part

of the inferior pulvinar (Mm Vc 16 and Mm Vc 21) whilst the more peripheral part of the visual field is represented more medially (Mm Vc 17 and Mm Vc 22).

This maintenance of a strict topographical organisation from the retina as far as the inferior pulvinar is very interesting as such organisation is usually a feature of primary afferent centres such as the lateral geniculate body, medial geniculate body and nucleus ventralis posterolateralis, and not of the association nuclei and association cortex (Truex and Carpenter, 1969).

(b) The Projection to the Lateral Geniculate Body

The degenerated fibres observed in the lateral geniculate body following lesions of the occipital cortex did not have the typical appearance of preterminal degeneration. In addition to the large fragmented degeneration fibres a rather unusual phenomanena was observed. Silver impregnated neurons were seen scattered throughout the part of the lateral geniculate body which showed retrograde degeneration on Nissl sections. From studying animals which had survived post-operatively for different lengths of time, we gained the impression that the impregnated neurons were more abundant in animals which had survived for a short period, while in animals which had survived for longer

periods the number of silver impregnated neurons were much reduced.

Thus in cases with a 6 day post-operative survival period (Mm Vc 17 and Mm Vc 18) silver impregnated neurons surrounded by irregular argentophilic fragments were seen. In the cases surviving for 7 days (Mm Vc 19 and Mm Vc 20) occasional degenerated fibres were present as well as the above mentioned argentophilic fragments and neurons. In the cases with a survival period of 11 days (Mm Vc 21 and Mm Vc 22) the number of argentophilic fragments and the number of impregnated neurons were reduced, but there were many degenerated fibres. In the three cases with survival periods from 13 to 15 days (Mm Vc 5 and Mm Vc 7) the silver impregnated neurons were few and far between, but degenerated fibres were quite numerous. Silver impregnated neurons similar to those in the lateral geniculate body were described by Grant and Aldskogius (1967) and Grant (1968), in the nucleus of the hypoglossal nerve and ventral spinal horn in cats, after sectioning of the nerve trunk or ventral roots. It would therefore appear that silver impregnation of neurons undergoing retrograde degeneration does occur.

From the findings of van Gehuchten (1903) with the Marchi method, and Cowan et al. (1961) with the Nauta method, we know that retrograde degeneration starts at

the cell body and progresses towards the periphery. Further, retrograde fibrillar degeneration mainly affects thick fibres, and appears as a dust-like pericellular precipitate in Nauta sections in the early stages. As the retrograde degeneration advances, thick single degenerated fibres and later fibre bundles appear in silver impregnated sections (Beresford, 1961; Guillery, 1967; Montero and Guillery, 1968). These findings seem to be very similar to our findings in the lateral geniculate body.

We have therefore, somewhat reluctantly, come to the conclusion that we have only demonstrated retrograde degeneration in the lateral geniculate body. The presence of retrograde degeneration is quite understandable considering the large geniculo-cortical projection, but it is the absence of anterograde degeneration which is difficult to accept because the cortico-geniculate projection has been well documented by Szenthàgothai, Hámori and Tömböl (1966) and Garey, Jones and Powell (1968) in the cat.

Garey et al. (1968) were very conscious of the difficulty of differentiating between retrograde and anterograde degeneration. They came to the conclusion that the earlier appearing degeneration observed by them, in the dorsal lateral geniculate body in Nauta stained

material, was most probably anterograde in nature, but that an electron microscopical study would be necessary to determine this with certainty. Such electron microscopical observations have been described by Szentàgothai, Hámori and Tömböl (1966) and were quoted as unpublished observations of their own by Garey et al. (1968). Their conclusion that the earlier appearing degeneration is anterograde in nature supports the opinion of Guillery (1967) that the cortico-geniculate system degenerates quickly following a cortical lesion, while the geniculo-cortical system undergoes retrograde degeneration at a later stage.

In the cat the topographical organisation of the geniculo-cortical projection is identical to that of the cortico-geniculate projection (Guillery, 1967). Because of this point to point reciprocity in the geniculo-cortico-geniculate system it is not possible to differentiate between anterograde and retrograde degeneration on a topographical basis. We are therefore dependent on an unequivocal demonstration of degenerated boutons. No large degenerated boutons were seen in sections stained with the Glees (1946) method, but it is well known that this method effectively shows degenerated boutons in certain systems only.

We therefore came to the same conclusion as Garey et

al. (1968) did, namely that an electron microscopical investigation is essential to determine the presence of a cortico-geniculate projection. This investigation will be dealt with in the next chapter.

(c) The Projection to the Tectum

Degeneration was seen in the superficial three layers of the tectum opticum following lesions of areas 17, 18 and 19. This confirms the findings of Wilson and Toyne (1969) in the Macaca mulatta and of Garey et al. (1968) in the cat.

The projection from area 17 to the superior colliculus appears to be topographically organised, because the position of the degenerated fibres in the tectum varied with differently placed cortical lesions.

The projection of the retina to the superior colliculus is organised in the same way as the retino-geniculate projection. Therefore both the lateral geniculate body and the superior colliculus of one side are activated by stimuli from the contralateral visual field. The retino-tectal projection is organised in such a way that the horizontal meridian of one hemifield extends through the superior colliculus from antero-laterally to postero-medially. Medial to the meridian lies the upper

visual hemifield and lateral the lower hemifield. This organisation was demonstrated electrophysiologically by Whitteridge (1960) and confirmed by the neuroanatomical investigation of Wilson and Toyne (1969), both in the Macaca mulatta.

Further, Wilson and Toyne (1969) were also able to show that the cortico-tectal projection in the rhesus monkey is organised in such a way that the cortical area which receives impulses from a particular retinal area, projects to the same tectal area as the retinal area in question. These findings were similar to those of Garey et al., (1968) and Garey and Powell (1968) in the cat. Our findings confirm the findings of Wilson and Toyne (1969).

In our material we were able to observe both an oro-caudal as well as a latero-medial organisation. The most oral termination of degenerated fibres in the tectum was seen in case Mm Vc 21 in which the cortical lesion was the closest to the cortical representation of the fovea centralis. The further the cortical lesion was removed from the cortical representation of the fovea, the more posteriorly placed was the resulting degeneration in the tectum. The distribution of degenerated fibres in the tectum in the remaining cases was from anterior to posterior in the following order: Mm Vc 18, 20, 19, 17 and most posteriorly,

Mm Vc 22.

As regards the latero-medial organisation of the cortico-tectal projection, we were able to show that in those cases in which the lesion was situated in the cortical area representing the lower visual hemifield the resulting degeneration occurred in the lateral part of the tectum (cases Mm Vc 21, 16, 18, 20 and 17). In cases Mm Vc 19 and Mm Vc 22, where the lesion involved the cortical representation of the upper visual hemifield the area of degeneration in the tectum was medial to the position of the horizontal meridian.

(d) The Projection to other Subcortical Areas

(i) The Pregeniculate Nucleus

Our findings of a cortico-pregeniculate projection from areas 17, 18 and 19 confirm the findings of Campos-Ortega (1968) in the Galago crassicaudatus. Because the n. praegeniculatus of primates is a homologue of the subprimate ventral lateral geniculate body, our findings also confirm those of Garey et al. (1968), of a projection from the visual cortex to this nucleus in the cat.

(ii) The Pretectal Area

Our findings of a projection from the occipital

cortex to the pretectal area confirm the findings of Kuypers and Lawrence (1967) in the Macaca mulatta and Campos-Ortega (1968) in the Galago crassicaudatus. This projection also appears to be topographically organised. Thus medially placed occipital lesions resulted in ventrally situated degeneration in the pretectum while oro-ventral lesions resulted in dorsally situated degeneration.

(iii) Nucleus Reticularis Thalami

After large lesions a fair amount of terminal degeneration was seen in this nucleus (Mm Vc 5, Mm Vc 6, Mm Vc 7). A connection from the visual cortex to the nucleus reticularis thalami has been described by Biemond (1929) in the rabbit, Gerebetzoff and Wouters (1941) in the guinea pig, Beresford (1961), Guillery (1967) and Garey et al. (1968) in the cat, and by Campos-Ortega (1968) in the Galago crassicaudatus.

(iv) Nucleus Lateralis Dorsalis

Only the para- and peri-striate parts of the visual system appear to project to this nucleus. Terminal degeneration was found in this nucleus after lesions involving areas 18 and 19 (cases Mm Vc 6 and Mm Vc 7) whereas it was absent in cases

where the lesion was restricted to area 17. This projection has not been described before. It is important insofar as it shows the presence of a connection between the peri- and para-striate cortex and a nucleus of the limbic system (Locke, Angevine and Yakovlev, 1961). The nucleus lateralis dorsalis has been shown to project to the parasplenial limbic cortex in the cat by Locke, Angevine and Yakovlev (1961) and by ourselves. This projection has also been described in the monkey (Locke et al., 1964; Yakovlev et al., 1966) and in man (Locke et al., 1961; Yakovlev et al., 1966).

(v) Zona Incerta

After both large and small lesions of the visual cortex, degeneration was found in the zona incerta. In some cases these fibres continued to the nucleus rubor where they terminated in the pars parvocellularis. This projection has been described in primates by Kuypers and Lawrence (1967) and Campos-Ortega (1968).

(vi) Nucleus Caudatus

After large occipital lesions affecting the peri- and para-striate areas degeneration was found in the posterior part of the body of the caudate

nucleus. Such a projection was also seen in the cat by Webster (1965) and in the Galago by Campos-Ortega (1968).

(vii) Pons

Our finding of a projection from all three visual areas (17, 18 and 19) to the laterodorsal part of the griseum pontis, confirms the findings of Nauta and Bucher (1954) in the rat, Garey et al. (1968) in the cat, and Campos-Ortega (1968) in the Galago.

(viii) Nucleus Tractus Opticus Accessorius

This nucleus, described by Giolli (1963), Campos-Ortega and Glees (1967) and Campos-Ortega and Cluver (1968) in various primates receives accessory optic fibres and appears to be the homologue of the lateral terminal nucleus of the accessory optic system of subprimates (Heyhow, 1959 and 1966; Heyhow et al., 1960).

A small number of terminally degenerated fibres were seen in this nucleus after occipital lesions. This confirms the findings of Garey et al. (1968) in the cat and Campos-Ortega (1968) in the Galago. The significance of a cortical input to this nucleus

remains unknown as does the function of the whole accessory optic system.

C H A P T E R V I

ELECTRON MICROSCOPICAL INVESTIGATION OF THE PROJECTION FROM THE VISUAL CORTEX TO THE PULVINAR, LATERAL GENICULATE BODY AND THE TECTUM

VI.1 GENERAL

(a) The Purpose of this Investigation

In the previous chapter it was shown that it is very difficult to determine whether degenerated fibres have undergone retrograde or anterograde degeneration if the terminal part of the fibre is not adequately demonstrated. In such cases, especially if the problem is further increased in complexity by the presence of retrograde degeneration in Nissl sections, an unequivocal answer can only be obtained by an electron microscopical investigation.

We have studied the cortico-geniculate projection electron microscopically, and at the same time the cortico-pulvinar and cortico-tectal projection. The cortico-pulvinar and cortico-tectal projections

served as additional control material as these projections are well established. Particular attention was paid to the ultrastructure of the primate pulvinar, and the mode of termination of degenerated boutons in this nucleus.

(b) The Electron Microscopical Appearance of the Normal Pulvinar

Until now the pulvinar has only been studied electron microscopically in the cat (Majorossy, Rethelyi and Szentàgothai, 1965; Hirata, 1966) and to the best of our knowledge no electron microscopical studies on the primate pulvinar have been published.

In the cat the dominant feature of synaptic organisation in the pulvinar is the presence of synaptic glomeruli. According to Majorossy et al. (1965), these glomeruli have the following appearance: The glomerulus is round or oval and has a diameter of 5-6 microns. It is surrounded by a thin glial capsule through which the pre- and post-synaptic elements pass. The centre is occupied by a large coarse dendritic profile which is surrounded by closely packed terminal axon profiles. There are numerous synaptic contacts between the axons and the central dendrite.

Another characteristic feature of the pulvinar is the common occurrence of axo-axonal synapses especially between small axons as the pre-, and large axons as the post- synaptic element. The findings of Hirata (1966) are very similar to those of Majorossy et al. (1965) as far as the synaptic organisation is concerned. Hirata (1966) however recognised two types of synaptic vesicles according to whether they have a spherical or cylindrical shape. The axon terminals were classified into three types; type a, small terminals containing spherical vesicles; type b, large terminals containing cylindrical vesicles, and type c, rather rare mossy endings. According to Hirata the three types of axon terminals described by him correspond to the three types recognised by Majorossy et al. (1965). They are the following:

(i) Large axon terminals containing numerous mitochondria, but very few synaptic vesicles. These correspond to the type b endings of Hirata.

(ii) Relatively large axon terminals which were densely packed with mitochondria and synaptic vesicles. These correspond to the type c endings of Hirata.

(iii) Small axon terminals containing a moderate number of mitochondria and synaptic vesicles. These correspond to the type a terminals of Hirata.

TABLE VI

Post-operative survival times of animals used for electronmicroscopy.

Mm Vc 1	2 days
Mm Vc 2	2 days
Mm Vc 3	3 days
Mm Vc 8 & 9	4 & 11 days
Mm Vc 10 & 11	5 & 24 days
Mm Vc 12 & 13	6 & 9 days
Mm Vc 14 & 15	7 & 150 days
Mm Vc 23 & 24	48 & 48 days

VI.2 MATERIAL AND METHODS

The material for the electron microscopical investigation consisted of 8 normal young adult Macaca mulatta with bodyweights ranging from 7 Kg. to 9 Kg.

(a) Anaesthesia

The animals were anaesthetised with Fluothane using the open drip method. This allowed quick induction as well as easy control over the level of anaesthesia.

(b) Operation

Seven of the eight animals were operated on. One was not operated on as a control. In two cases bilateral occipital lobectomy was performed, in each as a single procedure. In each of the remaining five the occipital lobes were removed in two stages separated by several days, in order to obtain different post-operative survival times in the same animal.

At each operation a large craniectomy was performed over the sulcus lunatus (simian sulcus). The brain was incised by aspiration immediately anterior to this sulcus down to the tentorium cerebelli. In this way areas 17, 18 and the greater part of area

19 were completely isolated. A thin strip of area 19 was left intact anterior to the lesion to ensure that necessary coagulation of blood vessels would not damage the adjacent areas 7, 22, 21 and 20. In all cases the dura was sutured to avoid herniation of the brain. The post-operative survival times are given in table VI.1.

(c) Perfusion

The method of perfusion was essentially the same as that described for the pig in Chapter IV. The main differences were, firstly, that the fixing solution was preceded by a 10% rheomacrodex solution. The purpose of this was to wash out as much blood as possible and to avoid sludging in the small vessels. Without the rheomacrodex there tended to be more clotting of the blood in small vessels. Secondly, different fixing solutions were used. In half of the cases glutaraldehyde (Sabatini, Bensch and Barnett, 1963) was used and in the other half a mixture of glutaraldehyde and paraformaldehyde (Karnovski, 1961).

Immediately after perfusion the brain was removed and the pulvinar, lateral geniculate body and tectum opticum dissected out. These structures were cut into small blocks which were post-fixed in Dalton's solution and thereafter embedded in Vestopal.

Fig. VI.1

The electron micrograph shows a normal glomerulus of the inferior pulvinar of a Macaca mulatta.

The glomerulus consists of a dendrite surrounded by axon terminals. The axons are marked Ax and the dendrite Den. Synapses are pointed out by arrowheads.

Fig. VI. 1. A normal glomerulus in the inferior pulvinar.

Fig. VI.2

The electron micrograph shows a section of the inferior pulvinar of a Macaca mulatta. In the centre a large axon undergoing fibrillary degeneration can be seen. The axon is marked DAx. On the left of the degenerating axon a normal axon, marked Ax, can be seen.

Fig. VI. 2. A axon (DAx) in the inferior pulvinar showing fibrillary degeneration.

(d) Sectioning and Staining

The blocks were sectioned with a L.K.B.ultra-microtome and the sections stained using either procedure II of Karnovski (1961) or the lead citrate method of Reynolds (1963). The sections were examined with a Zeiss EM 9 A electron microscope.

VI.3 RESULTS

(a) The Pulvinar

The characteristic synaptic unit in the pulvinar consisted of a glomerulus. Sections of a glomerulus (fig. VI.1) showed numerous axonal profiles and one or two dendritic profiles. In none of our sections a dendrite occupied a strict central position. In addition to the axodendritic synapses, a large number of axo-axonal synapses were also present.

Four days after operation the first axons showing fibrillar hypertrophy were seen (fig. VI.2). The individual fibrils appeared normal, but they were increased in number and appeared in small bundles scattered throughout the axon. The number of synaptic vesicles in these axons seemed to be reduced. This reduction in vesicles was probably only apparent and due to the swelling of the axon terminal. The

Fig. VI.3

The electron micrograph shows a normal optic axon in the lateral geniculate body of a Macaca mulatta. The optic axon is marked OAx. Arrowheads point to axo-axonic synapses occurring between small axon terminals and the large optic axon.

Fig. VI. 3. A normal optic axon (OAx) in the lateral geniculate body. Arrows point to axo-axonic synapses.

Fig. VI.4

The electron micrograph shows a section of the lateral geniculate body of a Macaca mulatta. Normal axones are marked Ax. Glia cells are marked Gl.

The dendrites in the section have an electron dense, irregular and shrunken appearance. These are pointed to by arrowheads.

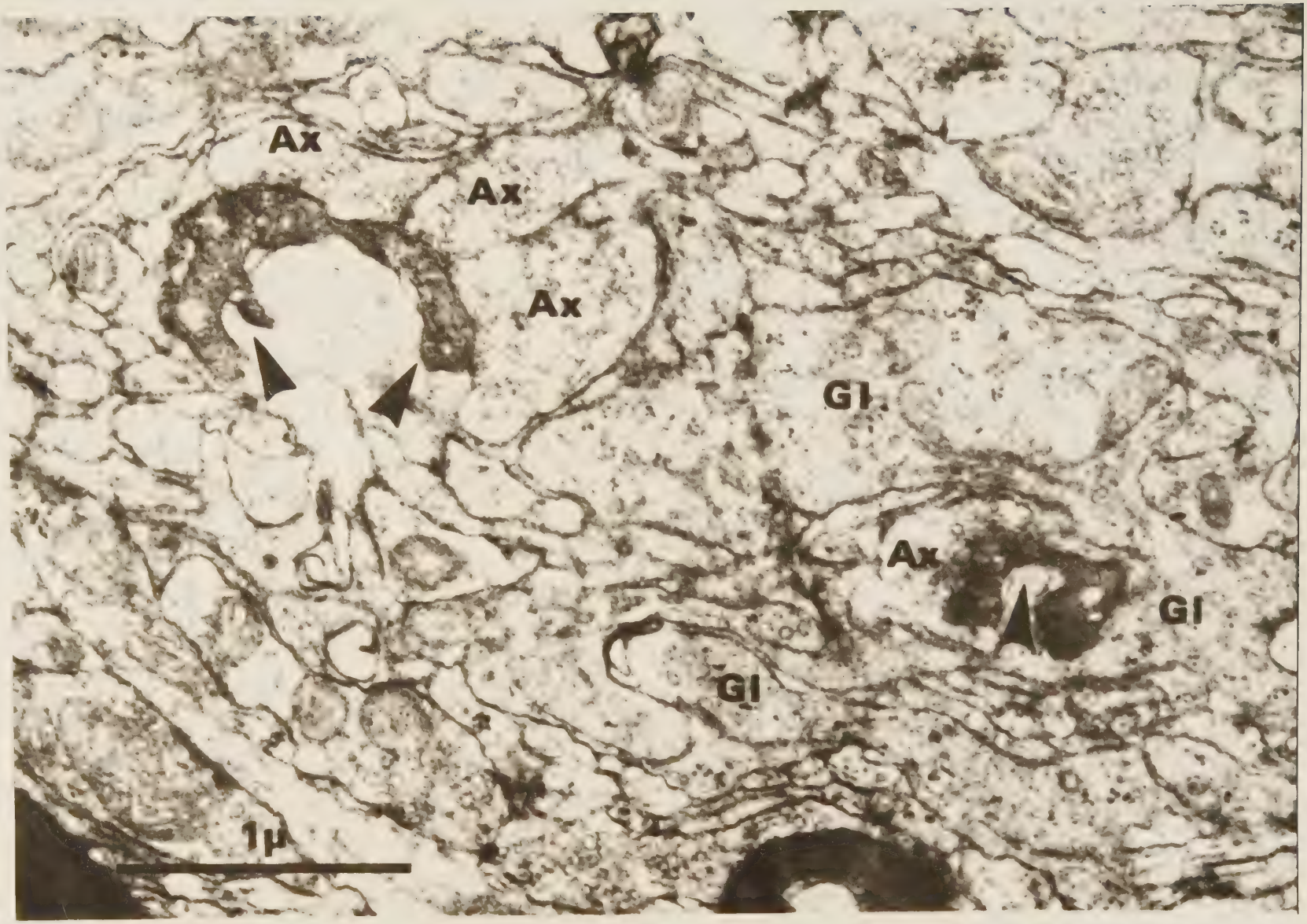


Fig. VI. 4. Axodendritic synapses in the lateral geniculate body showing degeneration of the postsynaptic component. Abreviations : Ax: axon; GL: glia.

mitochondria in these axons had a normal appearance. These changes were only present in animals which had survived between 4 and 9 days. Such axon terminals were no longer present where the survival period was 11 days or longer.

(b) The Lateral Geniculate Body

In animals with a post-operative survival period of two days, no changes were seen. After a three day survival period, the first changes were noted. These consisted of very electron-dense, post-synaptic profiles. The profiles had an irregular shrunken appearance and commonly contained large normal-looking mitochondria. Frequently the profiles were partially or completely surrounded by glia-prolongations (fig. VI.4). These profiles became more numerous in animals surviving from three to seven days, and decreased in number in animals surviving for nine days. In animals with a post-operative survival period of eleven days and longer, these dark profiles were no longer observed. Disintegrated neurons were observed in all the material which contained the dark post-synaptic profiles. These neurons contained irregularly distributed vacuoles throughout the cytoplasm and a nucleus could be recognised (fig. VI.5). The

nuclei of these disintegrated neurons showed signs of degeneration such as fragmentation and dissolution of the nuclear membrane.

(c) The Tectum

The material investigated was limited to the stratum zonale and griseum superficiale of the superior colliculus.

The first signs of degeneration were seen in material with a post-operative survival period of four days. The characteristic change in this material consisted of axonal profiles with a dark shrunken appearance. These profiles were filled with densely packed synaptic vesicles. In these dark axon terminals, pre-synaptic thickening was still intact and was very prominent. The axons showing these changes were small and medium sized and formed only axodendritic synapses. These axonal changes were no longer present in material which had survived for eleven days or longer post-operatively.

VI.4 DISCUSSION

In each of the three nuclei examined electron microscopically, different abnormal structures were seen. In the pulvinar there were axon terminals which showed increased

Fig. VI.5

The electron micrograph shows a section of the lateral geniculate body of a Macaca mulatta. The centre of the section is occupied by a disintegrated neuron which has a dark, irregular and shrunken appearance. Vacuoles are irregularly distributed throughout the cytoplasm. The disintegrated neuron, or Fink-Heimer cell, is surrounded by glia cells marked Gl.

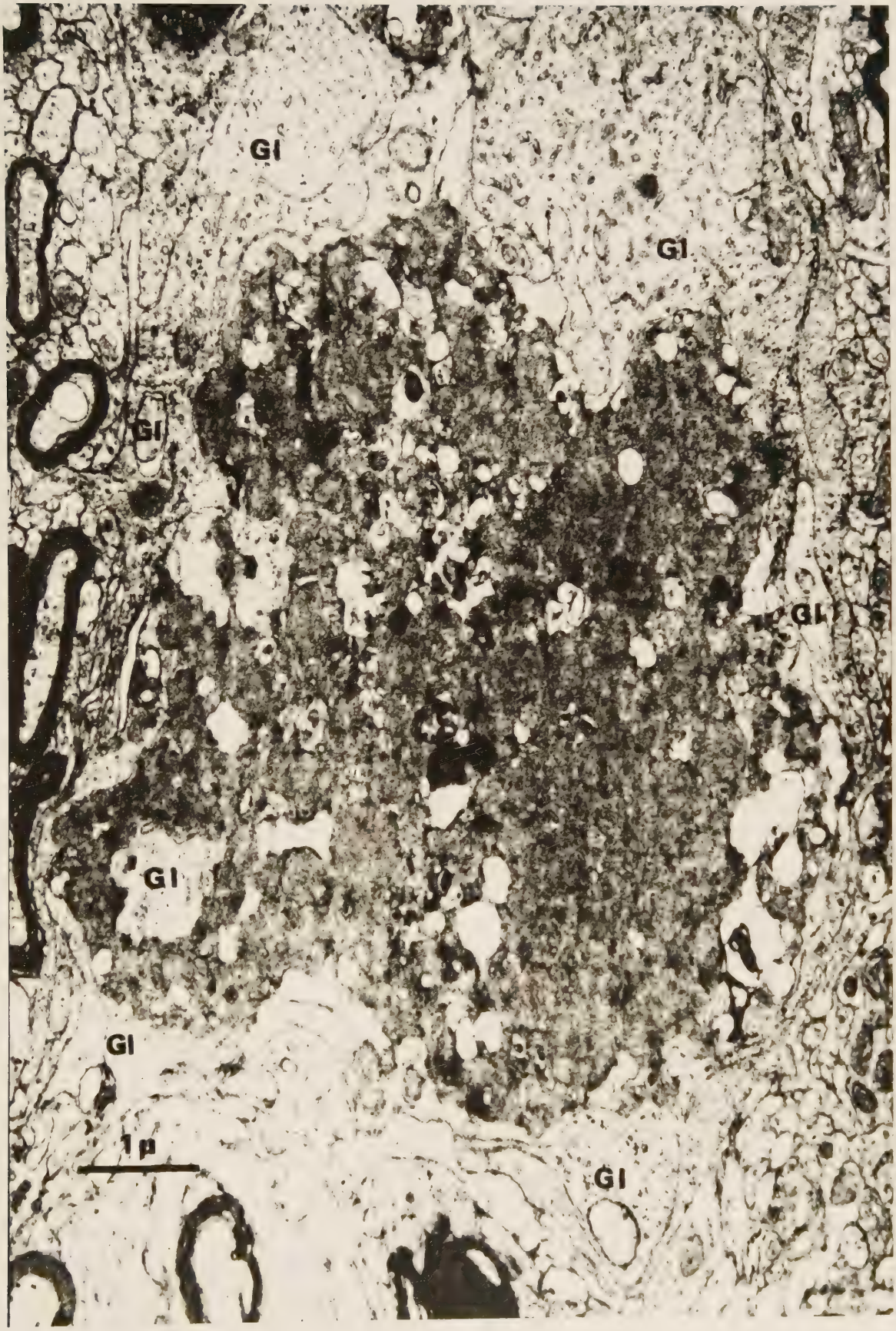


Fig. VI. 5. A Fink-Heimer cell surrounded by glia cells (GL).

numbers of neurofibrils, in the tectum there were axon terminals with a dark shrunken appearance and in the lateral geniculate body post-synaptic structures with a shrunken, irregular, vacuolated appearance surrounded by glia.

The changes observed in the pulvinar and tectum correspond with the two major patterns of change in degenerating axon terminals described in the literature as filamentous and non-filamentous (or dark) modes of degeneration.

The proliferation of neurofilaments in pre-synaptic structures after section of the relative axon has been described in the optic tectum (Gray and Hamlyn, 1962), the lateral geniculate body (Collonnier and Guillery, 1964; Smith, O'Leary, Harris and Gray, 1964; Guillery, 1965; Glees, Meller and Eschner, 1966; Szentàgothai, Hamori and Tömböl, 1966), the superior colliculus (Lund, 1969), spinal cord (Ralston, 1968), lateral vestibular nucleus (Mugnaini and Walberg, 1967), the cerebellum (Smith, Hudgens and O'Leary, 1966) and in the olfactory cortex (Westrum, 1969). These filaments may appear as new structures, as is the case in the optic tectum, or they may dramatically increase in number as in the lateral geniculate body where they are also seen in some

of the normal pre-synaptic bags.

The presence of numerous neurofilaments in boutons has been postulated as the basis for argyrophilia occurring with neurofibrillar silver stains (Boycott, Gray and Guillery, 1961; Gray and Guillery, 1961; Lund and Westrum, 1966 a).

The validity of neurofilamentous hypertrophy as an electron microscopical manifestation of degeneration has been questioned by McMahon (1967) who regarded the dark, shrunken granular appearance as the only true appearance of degeneration. According to Saavedra, Vaccarezza and Mascitti (1969), the filaments observed in filamentous degeneration have all the characteristics of normal neurofilaments. The increase in neurofilaments during degeneration is the result of an "abortive attempt to regenerate" according to Gray and Guillery (1966).

In some parts of the nervous system neurofilamentous proliferation does not appear to be a significant part of the degenerative process. In these cases degenerating axon terminals have a dark (electron-dense) granular appearance and there is active phagocytosis by glial cells (McMahon, 1967; Westrum, 1969). The best example of an area in which filamentous degeneration does not occur is the cerebral cortex (Evans and Hamlyn, 1956;

Smythies and Inman, 1960; Westrum, 1969). Furthermore it should be noted that neurofilaments do not occur in cortical nerve endings in normal material (Gray, 1959; Collonnier, 1964).

(a) The Pulvinar

In the pulvinar we observed fibrillar changes in the terminal boutons of animals surviving between four and nine days post-operatively. These changes have the appearance of fibrillar degeneration described by other authors and reviewed above. These electron microscopical findings therefore corroborate the light microscopical finding presented in the previous chapter of an occipito-pulvinar projection.

A striking feature of the ultrastructure of the pulvinar is the glomerulus. This structure corresponds to some extent to the glomerulus of the cat pulvinar described by Majorossy et al. (1965) and Hirata (1966). The main difference between the glomeruli of the cat and the primate seems to be that the primate glomerulus is less rigidly organised. Unlike the glomerulus described by Majorossy et al.(1965) we found no constant central dendrite. We were also unable to demonstrate such a well defined glial capsule surrounding the glomerulus. In other respects the cat

and primate glomeruli compared closely. Thus we also observed numerous axo-axonal synapses and the general appearance of the glomeruli were very similar to those described in the cat.

Glomeruli have been described in the cerebellum of the cat by Hamori and Szentàgothai (1966), in the lateral geniculate body of the cat by Szentàgothai (1962; 1963), in the lateral geniculate body of the rhesus monkey by Campos-Ortega, Glees and Neuhoff (1968), and in the pulvinar of the cat by Majorossy et al. (1965). Glomeruli have also been described by Akert and Steiger (1967) in the neuropil of the ant brain.

Glomeruli are not found throughout the brain of vertebrates, but appear to be restricted to certain nuclei (Collonnier, 1966). It therefore seems reasonable to assume that glomeruli have a particular function in the central nervous system. This function according to Akert and Steiger (1967) and Majorossy et al. (1965) is one of integration of information at a cellular level.

(b) <u>The Lateral Geniculate Body</u>

No boutons showing either filamentous or non-

filamentous degeneration were observed in the lateral geniculate body. The electron-dense profiles and degenerated neurons observed in material surviving from three to nine days post-operatively were regarded as signs of retrograde cellular degeneration. This conclusion is based on the findings of Grant and Aldskogius (1967), Grant (1965), and Grant and Westman (1967; 1968). These findings would therefore corroborate the light microscopical findings in the lateral geniculate body described in the previous chapter. It should be noted that the time sequence in the appearance of degenerated disintegrating neurons shown electron microscopically, corresponds with the appearance and disappearance of silver impregnated neurons seen light microscopically.

(c) The Tectum

The presence of boutons showing the dark or non-fibrillar type of degeneration in the optic tectum confirms the findings of Lund (1969) in the rat, and the light microscopical findings presented in the previous chapter of an occipito-tectal projection.

CHAPTER VII

DISCUSSION

Each of the preceding chapters has dealt with a particular connection or group of connections of the pulvinar. In this, we will discuss how our findings influence the present concept of the functional significance of the pulvinar as a whole.

Functionally the pulvinar cannot be regarded in isolation, but must be viewed as an intrinsic part of the thalamus. We will therefore briefly consider the function of the thalamus in general before turning, more specifically, to the pulvinar.

VII.1. A Functional Classification of the Thalamus

The function of the thalamus is more complex than that of a simple relay station, or even a sensory integrating mechanism (Truex and Carpenter, 1969). The thalamus may be subdivided into three groups of nuclei on the basis of their function. These nuclear groups are not only functionally distinct, but also differ in their phylogenetic and ontogenetic identity. The three groups will be considered in their phylogenetic order and the discussion

confined to the general function of each group and not to the function of specific nuclei. The classification used is that of Yakovlev (1969) which is similar to those of Truex and Carpenter (1969) and Rose and Woolsey (1949).

Group I consists of the paraventricular, intra-laminar and reticular nuclei. Rose and Woolsey (1949) also included the habenular and pretectal nuclei in this group, but the former is now generally regarded as epi-thalamus and the latter as part of the mesencephalon (Ranson and Clarke, 1958; Humphrey and Lauer, 1962; Truex and Carpenter, 1969). The nuclei of this group are the oldest thalamic nuclei and form the paleothalamus, which makes up most of the thalamus of lower vertebrates such as reptiles and amphibians. In primates these nuclei are small relative to other thalamic nuclei.

The nuclei of group I are the first thalamic nuclei to develop in ontogeny, and appear early in the second month of development in the mantle layer of the dorso-lateral wall of the diencephalic vesicle in man (Yakovlev, 1969).

Although the para-ventricular and intra-laminar nuclei have no direct cortical connection (Nauta and Whitlock, 1954), the EEG arousal response is mediated by them. The character-istic response of these nuclei to stimulation is the

recruiting response described by Moruzzi and Magoun (1949), and Magoun (1952). These nuclei therefore play a major role in the regulation and maintenance of consciousness and attention by influencing cortical activity.

Group II consists of nuclei which relay information to specific cortical centres. The majority are specific sensory relay nuclei such as the two lateral geniculate bodies and the nuclei ventralis, postero-lateralis and medialis. Included in this group also is nucleus ventralis lateralis, which relays information from the cerebellum. The limbic nuclei also belong to this group and consist of the nucleus ventralis anterior, nucleus medio-dorsalis, nucleus anterior (all three divisions) and nucleus lateralis dorsalis.

Phylogenetically and ontogenetically these nuclei develop later than those of group I. They form the greater part of the thalamus of those primitive mammals in which the sensorimotor cortex comprises most of the cortex. The nuclei belonging to this group are the classical relay or integrating nuclei of the thalamus, but their function is probably more complex in most cases. Thus these nuclei are thought to be responsible for crude awareness of sensations such as touch and temperature and for the affective quality of these sensations. Recognition of

pain is also thought to occur, at least partly, at a thalamic level. This conclusion appears to be supported by the occurrence of dysesthesia in patients with thalamic lesions.

Group III consists of the association nuclei, namely the pulvinar and nucleus lateralis posterior. Phylogenetically and ontogenetically these two nuclei develop late. Of these two nuclei, Grünthal (1934; 1945) found only a rudimentary nucleus lateralis posterior in rodents. Despite its absence in rodents, the pulvinar develops rapidly in phylogény to become the largest of all thalamic nuclei in man (Walker, 1966).

The ontogeny of the pulvinar goes hand in hand with the dorso-lateral and posterior expansion of the cerebral hemispheres. At the fifth month of development, the pulvinar and nucleus lateralis posterior comprise but a quarter of the human thalamus, whereas at full term more than a third of the thalamus consists of pulvinar and nucleus lateralis posterior (Yakovlev, 1969).

Association nuclei are thought to receive no direct input from the ascending sensory systems, but to have abundant connections with other diencephalic nuclei and to project to the association cortex (Truex and Carpenter, 1969). These nuclei are presumed to integrate inform-

ation obtained from other nuclei and to project this integrated information to the association cortex. Cortico-thalamic fibres, so far as they have been demonstrated, are thought to exert an inhibitory effect upon the thalamus. This would allow cortical regulation of the integrative actions of the thalamus by selective inhibition (Truex and Carpenter, 1969). This concept is one of strict hierarchical levels where the higher level invariably has a more complex function, and controls the lower level. The position of the nucleus in the hierarchy clearly depends on its connections.

VII.2 The Connections of the pulvinar

It is generally accepted that the association nuclei are widely connected to other diencephalic nuclei (Truex and Carpenter, 1969). The association nuclei like the pulvinar, are thought to obtain information from specific thalamic nuclei like the lateral geniculate body and medial geniculate body, and project this integrated information to the association cortex (Hassler, 1959). These connections between the pulvinar and other thalamic nuclei may very well exist, but it should be remembered that such connections have not yet been demonstrated experimentally.

The reason for this is that a lesion of a thalamic nucleus close to the pulvinar would invariably damage

fibres from the cortex passing through the nucleus on their way to the pulvinar. It would therefore be impossible to distinguish between degenerated fibres arising from different nuclei or cortical areas.

The suggestion of Hassler (1959) that the pulvinar receives visual and auditory information from the two geniculate bodies, where it is integrated and then relayed to the association cortex, is very attractive, but still quite hypothetical.

In the light of this hypothesis we find it very interesting that we were able to demonstrate a large projection from the primary and secondary visual areas to the pulvinar. This finding, together with the findings of Whitlock and Nauta (1956) of a large projection from the temporal lobe to the pulvinar, indicates to us that the most significant afferent connections of the pulvinar are derived from the cortex. Could it be that the proposal of Hassler (1959) is basically correct in that the pulvinar relays integrated visual and auditory information to the association cortex, but that the auditory and visual information does not reach the pulvinar directly from the two geniculate bodies, but from the visual and auditory cortex ? Before we attempt to answer this question we shall reconsider the connections of the pulvinar.

(a) The Retino-pulvinar Projection

This projection was shown to exist only in simians of the animals examined. The retinal fibres terminated along the inferior lateral border of the inferior pulvinar. The cells on which the retinal fibres terminated were distinctly different in appearance from cells in any other part of the pulvinar. There is also evidence that these cells, unlike all other neurones in the pulvinar, do not project to the cortex (Walker, 1938a,and Peacock and Coombs, 1965). For these reasons we are inclined to regard the cells of the inferior pulvinar receiving a retinal projection as functionally separate from the pulvinar. We have no theory as to what their function could be, but the retinal projection to them is so small, compared to the occipito-pulvinar projection, that even if they were part of the simian pulvinar, it is unlikely that they are of major functional significance.

There is some evidence (Hassler and Wagner, 1965) that the retino-pulvinar projection becomes much larger in man and involves most of the inferior pulvinar. This is however based on a single case of anophthalmia and obvious degeneration anywhere in the pulvinar was not found by Minkowski (1920) after eye enucleation

in man. The extent of this projection has therefore not been clearly determined in man.

(b) The Pulvino-cortical Projection

(i) The Occipital Projection

The pulvinar of the cat was found to project to areas 18 and 19, but not to area 17. The largest projection was to area 19 and we were able to show that this projection was topographically organised.

In the primate, the pulvinar was also found to project to areas 18 and 19 by Le Gros Clarke and Northfield (1937), Chow (1950), and Hassler (1965). These authors found that it was mainly the inferior pulvinar which projected to areas 18 and 19, although a part of the lateral pulvinar was also found to project to areas 18 and 19.

The pulvinar in man projects to the secondary visual cortex (areas 18 and 19) according to Hassler (1959).

(ii) The Temporal Projection

In the cat we were able to demonstrate a

projection from the pulvinar to the antero-ventral part of the middle ectosylvian gyrus. This is part of the secondary auditory cortex of the cat, or area A II. We were unable to find any sign of a topographical organisation of this projection, but it is possible that the lesions in the pulvinar were too large for such organisation to be apparent.

In the primate, the pulvinar projects to the superior temporal gyrus (area 22), and part of the middle temporal gyrus (area 21) according to Chow (1950), Bucy and Klüver (1955) and Locke (1960). Area 22 is a possible homologue of the feline secondary auditory area, A II. The pulvino-temporal projection shows a very distinct topographical organisation according to the work of Chow (1950) and Locke (1960). These authors also found that it was only the posterior part of the middle pulvinar which projected to the temporal lobe.

A projection from the pulvinar to the posterior part of the temporal lobe in man was described by Hartmann and Simma (1952) and Simma (1954). Such a projection has also been described by Hassler (1959). The findings in man are however not

sufficient or detailed enough to allow an exact demarcation of this projection.

(iii) The Parietal Projection

It was already noted by Walker (1938 b) that the pulvinar has an extensive projection to the cortex anterior to area 19. This would mean areas 40, 39 (supramarginal and angular gyri) and area 37. These cortical areas are only found in man. In the rhesus monkey area 19 borders directly on areas 22, 21 and 20. Although a pulvino-parietal projection forms an important part of the pulvino-cortical projection in man (Walker, 1938 b; Hartmann and Simma, 1952; Simma, 1954; Truex and Carpenter, 1969) such a projection does not exist in the rhesus monkey as the particular cortical areas (40, 39 and 37) are not present in simians.

(c) The Cortico-pulvinar Projection

(i) The Occipital Projection

In the cat it has been shown that area 17 projects to nucleus posterior, but not to the pulvinar (Altman, 1962; Garey, Jones and Powell, 1968). Area 18 projects to the pulvinar according

to Altman (1962) and area 19 according to Altman (1962) and Garey et al. (1968).

In the rhesus monkey we were able to demonstrate a significant projection from area 17 to the inferior pulvinar and from areas 18 and 19 to the lateral pulvinar. The projection from area 17 to the pulvinar in the rhesus monkey is an interesting finding as such a projection does not exist in the cat. If however the nucleus posterior is regarded as a homologue of the inferior pulvinar, as was suggested in Chapter VI, then this projection becomes easily understandable. The projection from area 17 to the inferior pulvinar becomes more significant if the absence of a projection from area 17 to the lateral geniculate body in the monkey is accepted. We were unable to demonstrate such a projection either by light or electron microscopical methods. This raises the possibility that the feed-back from area 17 to the lateral geniculate body is relayed via the inferior pulvinar. We have however been unable to find a plausible reason for such an indirect feed-back, especially because a direct feed-back (area 17 to the lateral geniculate body) has been demonstrated in the cat (Szentàgothai, Hamori and Tömböl, 1966; Guillery, 1967; Garey

et al., 1968). We feel that further speculation on the presence of a projection from area 17 to the lateral geniculate body in the cat and in the primate can serve little purpose at this stage of our knowledge. Before the findings on this projection are accepted more work needs to be done in both primates and sub-primates and greater clarity on the electron microscopical appearance of degeneration be obtained.

Our results clearly indicate that the projection from area 17 to the inferior pulvinar is topographically organised and that this organisation is related to the organisation of the retino-cortical projection. In our opinion, this degree of topographical organisation means that the function of this system is a highly discriminatory one.

The projection from areas 18 and 19 to the lateral pulvinar present no problem. It is by no means a unique primate characteristic, but is also found in the cat where the projection from area 19 to the pulvinar is also larger than that from area 18 (Majorossy, Réthelyi and Szentágothai, 1965).

It is stated by Truex and Carpenter (1969)

that areas 18 and 19 project to the pulvinar in man. This opinion appears to be based on the findings of Szentàgothai et al., 1966; Guillery, 1967; Garey et al., 1968; in cats. We have not been able to find any pathological or other studies in man to support this view.

(ii) The Temporal Projection

It has been shown by Niemer and Jiminez-Castellanos (1950) that areas AII, and Ep which form the secondary auditory areas of the cat, project to the pulvinar.

The temporo-pulvinar projection in the rhesus monkey has been extensively investigated by Whitlock and Nauta (1956). These authors found projections from the superior (area 22), middle (area 21) and inferior (area 20) temporal gyri to the pulvinar. The largest projection was from the superior temporal gyrus; a smaller projection existed from the middle temporal gyrus; and the projection from the inferior temporal gyrus to the pulvinar was relatively insignificant.

We have thus been able to show that the pulvinar receives its main afferent supply from the cortex and in turn projects back to the cortex.

The cortical areas involved in the primate are the primary and secondary visual areas and the secondary auditory areas on the afferent side, and the secondary visual and auditory areas on the efferent side.

When we look at the position of the pulvinar in the visual system, we find that the lateral geniculate body projects to area 17, which in turn projects to areas 18 and 19 (Truex and Carpenter, 1969). In the cat area 17 projects back to the lateral geniculate body and nucleus posterior, whereas in the monkey area 17 apparently only projects to the inferior pulvinar and not to the lateral geniculate body. The pulvinar projects to areas 18 and 19 and receives a projection from both these cortical areas. In man the pulvinar projects to the newly developed areas 37, 39 and 40 (Walker, 1938 b; Hartmann and Simma, 1952; Simma, 1954).

In the auditory system the medial geniculate body projects to areas 41 and 42, which in turn project back to the medial geniculate body and also to the adjacent area 22 (Truex and Carpenter, 1969). Areas 21 and 22 have a reciprocal connection with the pulvinar, whereas area 20

projects to the pulvinar, but does not receive a reciprocal projection (Chow, 1950; Bucy and Klüver, 1955; Locke, 1960; Hartmann and Simma, 1952; Simma, 1954; Hassler, 1959; Whitlock and Nauta, 1956).

On the basis of these connections it appears that the pulvinar is related in an indirect way to the visual and auditory systems. Its position in the hierarchy is not between specific thalamic nuclei and the association cortex, but between specific cortex and association cortex.

Electron microscopically we were able to demonstrate numerous synaptic glomeruli in the pulvinar, which according to Majorossy, Rethelyi and Szentàgothai (1965), and Akert and Steiger (1967), function as integration centres on a cellular level.

The connections and ultrastructure of the pulvinar appear to support the hypothesis of Papez (1939) and Hassler (1959), that the pulvinar is an integration centre of visual and auditory information, although this information is relayed to the pulvinar via the cortex and probably not directly from the geniculate bodies

as was proposed by these authors.

The very definitive topographical organisation of the cortico-pulvinar and pulvino-cortical projections give us some indication of the type of function with which the pulvinar is concerned. Generally it is found that afferent systems which are capable of fine discrimination (for instance, the visual system) show a very definitive topographical organisation, whereas this is not the case in systems mediating a more affective, less discriminatory sensation, such as pain (Yakovlev, 1969). We could reasonably expect, therefore, that the function of the pulvinar is in some way capable of fine discrimination.

In man a connection between the pulvinar and the parieto-temporal cortex has been described. This connection adds another dimension to the function of the pulvinar because we have some knowledge of the function of the parieto-temporal cortex, or specifically areas 37, 39 and 40. Before we had acquired our present knowledge about the connections of the pulvinar, von Bonin (1950) made the following statement referring to this cortical region. "Optic, acoustic and somesthetic areas all send impulses

into the parieto-temporal sector, the areas of which are directly or indirectly affected by the pulvinar of the thalamus. Many observations point to a predominantly gnostic function of this sector. We have no information about the impulses relayed by the pulvinar since its own afferents are unknown, nor are the details of this radiation well known."

It would seem as if the pulvinar only really becomes functionally important in man and that knowledge of the non-human pulvinar is of no help in determining the function of this nucleus in man.

VII.3. The Evolution of the Pulvinar

In the course of this work it has become clear that considerable differences exist between the pulvinar of the cat and that of the rhesus monkey, and again between that of the rhesus monkey and of man. These differences are so great that we cannot apply the findings obtained on the cat to man, or even to quite primitive primates. On the other hand, this does not mean that all our knowledge of the cat brain is useless in so far as it cannot contribute to our understanding of the human brain.

When a system or nucleus changes relatively little in

the course of evolution, as is for instance the case with the relay nuclei like the lateral and medial geniculate bodies, the findings in a sub-primate could be applicable to primates or even to man. There would be small differences between the species, but no basic functional difference.

When however the nucleus in question develops rapidly in phylogeny as is the case with the pulvinar, valid deductions may be drawn from a comparative anatomical series. The fact that a comparative study of different animals can contribute to our comprehension of apparently pure human functions was stressed by Elliot Smith as early as 1910. "I am not so foolish as to imagine that the evolution of the mind can be explained by anatomical studies; but I do maintain that without a correct comprehension of the homologies of the cerebrum in different vertebrates it will be impossible to make full use of the vast knowledge of comparative psychology which is now being built up, or fully to understand and interpret the varying behaviour of animals and the differences in their reactions to their environment." (Elliot Smith, 1910).

We know that the pulvinar appears late in phylogeny (Grünthal, 1934) and that certain subdivisions of the pulvinar are only found in man (Grünthal, 1934; Hassler, 1959; Yakovlev, 1969). The clue to the function of

the pulvinar lies in this very rapid development.

From its connections, we have deduced that the pulvinar is concerned in some way with the visual and auditory systems. From its phylogenetic development we may deduce that the pulvinar has no function in sub-mammalian vertebrates, that functionally it becomes of some importance in primitive mammals, is of course of considerable importance functionally in primates, and that the pulvinar has developed to such an extent in man that it has functions which do not exist in lower forms. We must therefore compare the behavious of different animals and man, and determine what man is able to do, that no animal can do, and what related function is most developed in the higher primates. This takes us outside the discipline of neuroanatomy and we will therefore only quote the opinions of Max Müller the comparative philologist, H. W. Magoun the neurophysiologist, and Konrad Lorenz the ethologist, without discussing their opinions.

"Where then is the difference between brute and man ? What is it that man can do, and of which we find no signs, no rudiments, in the whole brute world ? I answer without hesitation: the one great barrier between the brute and man is language. Man speaks, and no brute has ever uttered a word."

(Müller, 1861).

"Darwinian development, however, and its etiological relationship to Darwin's ideas does not seem previously to have been extensively examined. One cannot but be curious concerning the derivation of the views of Hughlings Jackson in neurology, of Pavlov in physiology, of Freud in psychiatry, and of Edinger in anatomy, each of which accounted for the phylogenetic elaboration of the central nervous system in terms of a series of superimposed levels, added successively as the evolutionary scale ascended.

"In each of these conceptual systems, the management of primitive, innate, stereotyped behaviour, having to do with the preservation of the individual and the race, was attributed to older, subcortical, neuraxial portions of the central nervous system, which formed Jackson's lowest level and subserved the Pavlovian unconditioned reflex and the Freudian id.

"Next, the more mutable, adoptive, learned behaviour of Pavlov's conditioned reflex, together with the capacity of the Freudian ego for perception and the initiation of movement were ascribed to higher neural structures, including the sensimotor cortex of Jackson's middle level, which developed above or upon the older subjacent parts.

"Finally, in the brain of man, hypertrophy of the associational cortices of the frontal and parieto-occipito-temporal lobes, forming Jackson's highest level, was

correlated with the capacities of Freud's superego and, in the dominant hemisphere, with the capabilities of Pavlov's second signal system for symbolization and communication by means of spoken and written language."

(Magoun, 1960).

"..... und es will scheinen, als ob diese engste Bindung zwischen Tun und Erkennen, zwischen Praxis und Gnosis ein besonderes Zentralorgan zur Voraussetzung hat, das nur der Mensch besitzt, und zwar in Gyrus supramarginalis der linken unteren Schläfenhirnwindung. Bei Verletzung dieser Hirnteile, in denen vielsagenderweise auch das Sprachzentrum liegt, treten beim Menchen neben Sprachstörungen bestimmte Ausfälle des Tuns wie des Erkennens, Apraxien und Agnosien auf, und es ist bisher nicht gelungen, bei Affen ähnliche Zentren nachzuweisen oder ähnliche Ausfälle hervorzurufen."

(Lorenz, 1965).

VII.4 Recent Physiological Findings in Man

In recent years much valuable experimental information about the thalamus has been obtained in the course of therapeutic stereotaxic procedures in man.

In a series of 28 patients undergoing thalamotomy for various disorders of movement, Ojemann, Fedio and Van

Buren (1968) were able to stimulate the pulvinar, while testing the patient with object naming tests. In these cases the electrode was left in place for ten days, which had the advantage that neither patient nor examiner were under the stress of operative conditions during the tests.

The position of the electrode was verified by the usual radiological methods. One patient of the above series died and so allowed anatomical verification of the position of the electrode. The authors found that stimulating the right pulvinar did not affect the patient's speech, but stimulation of the left pulvinar caused disruption of speech. The speech defect consisted of an inability to name objects and misnaming of objects.

To obtain further support for their theory that the pulvinar acts as a subcortical speech centre, these investigators conducted two further studies, one a pathological anatomical study of patients with aphasia (Van Buren and Borke, 1969), and the other a more extensive study of the effects of stimulation of the thalamus on speech (Ojemann and Ward, 1971).

Van Buren and Borke (1969) were able to show degenerative changes in the pulvinar in all cases which had presented with disturbances of speech. In addition they were also able to correlate the severity of the aphasia with

the extent of degenerative involvement of the pulvinar. These findings therefore confirm the earlier findings of Smyth and Stern (1938), McKissock and Paine (1958), and Cheek and Taveras (1966) in cases with tumours involving the pulvinar. A mixed type of aphasia has also been reported by Ciemins (1970) in two cases with primary intra-thalamic haematomas involving mainly the pulvinar.

In their study of speech representation in the ventro-lateral thalamus, Ojemann and Ward (1971) were able to confirm the earlier findings of Ojemann, Fedio and Van Buren (1968) that stimulation of the pulvinar causes anomia. In addition they were also able to show that stimulation of the medial central portion of the left ventro-lateral nucleus caused anomia. Beck and Bignami (1968) were able to show that lesions involving the central, medial and posterior parts of the ventro-lateral nucleus result in degeneration of fibres to the nucleus centrum medianum. From these findings it seems that anomia is not only elicited by stimulating the pulvinar but also by stimulating fibres ending in the nucleus centrum medianum. These findings fit the hypothesis of Penfield and Roberts (1959) according to which the angular and supramarginal gyri are connected to Broca's area via the pulvinar and nucleus centrum medianum. According to this hypothesis, cortical connections between the posterior and anterior speech areas do not exist, but

are of no great significance, because removal of the cortex surrounding the speech areas does not produce aphasia (Penfield and Roberts, 1959). The hypothesis of Penfield and Roberts has by no means been proven correct by these findings because the presumed connection between the nucleus centrum medianum and Broca's area has as yet not been demonstrated neuroanatomically. The findings of Ojemann's group have however clearly shown that the classical concepts of speech function, namely that it involves only cortical and immediate subcortical structures and that thalamic structures are not involved (Head, 1926; Neilsen, 1946) can no longer be regarded as adequate.

Our findings lend further support to this theory of speech function.

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SUMMARY

A study has been made of the connections of the pulvinar, and the possible functional significance of this nucleus has been re-evaluated. This evaluation has been based on the connections and the phylogenetic and ontogenetic development of the pulvinar.

The work falls into the following main parts:

1. The Retino-pulvinar Projection

This was studied in the Göttingen dwarf pig, in the prosimian Galago crassicaudatus, in Cebus cappucinus, in Macaca mulatta and in Papio ursinus. It has been shown in this study that a retino-pulvinar projection exists only in the higher primates. Such a projection was not found in the Galago or in the pig. In the pig a medial interlaminar nucleus and a nucleus posterior similar in appearance and position to these nuclei in the cat was found. The nucleus posterior was considered a possible homologue of the primate inferior pulvinar because it projects to area 19 and receives a retinal input.

2. The Pulvino-cortical Projection in the Cat

The major projection of the cat pulvinar is to area 19. It was found that this projection is topographically organised. Further it was shown that the pulvinar also projects to area 18, but that it does not project to area 17.

Although the most important efferent connection of the pulvinar appears to be to the secondary visual cortex, it was possible to demonstrate a discrete projection to part of the secondary auditory cortex, area AII.

3. The Cortico-pulvinar Projection in the Macaca mulatta

Unlike in the cat where the cortico-pulvinar projection arises solely from the secondary visual cortex, areas 18 and 19, the major cortico-pulvinar projection in the Macaca mulatta arises from area 17.

Area 17 projects mostly to the inferior pulvinar but also sends a few fibres to the lateral pulvinar. This projection is not reciprocal.

Because a projection from area 17 to nucleus posterior is known to exist in the cat, the demonstration of this projection in the Macaca mulatta lends additional support to the theory that the inferior pulvinar is a homologue of the subprimate nucleus posterior. Both areas 18 and 19

project to the lateral pulvinar and in both, this projection is reciprocal.

It was found that the projection from area 17 to the inferior pulvinar is topographically organised. This is part of a point to point organisation maintained throughout the visual system, starting from the retina. A similar organisation was found to exist in the cortico-tectal projection. The tectum receives fibres from areas 17, 18 and 19. The organisation is such as constantly to connect a point in the cortex to a point in the tectum related to the same part of the visual field. Although degenerated fibres were seen in the lateral geniculate body after lesions involving area 17, these were thought to be fibres undergoing retrograde degeneration. In addition to the degenerated fibres, degenerated neurons were also seen.

4. The Electron Microscopical Investigation

To obtain unequivocal proof of the nature of the degenerated fibres in the lateral geniculate body, an electron microscopical investigation of the cortico-pulvinar, cortico-geniculate and cortico-tectal projection was undertaken. This part of the work was done on the Macaca mulatta.

The synapses in the pulvinar were found to be organised in glomeruli similar to those described in the cat. Axons showing fibrillar degeneration were seen in the pulvinar in animals with a post-operative survival period of 4 to 9 days. No degenerated axons were seen in the lateral geniculate body, but degenerated dendrites and disintegrated neurons were seen. These were thought to be the result of retrograde degeneration. In the tectum degenerated axons with a dark shrunken appearance were seen after a post-operative survival period of 4 days.

The overall conclusions drawn from this work were as follows: The reciprocal connections of the pulvinar with the visual and auditory cortex indicates that the function of the pulvinar is to integrate visual and auditory information. The presence of synaptic glomeruli lends further support to the theory that the pulvinar functions as an integrating centre. The rapid development of this nucleus late in phylogeny, associated with the development of the temporo-parieto-occipital association cortex, suggests strongly that the function of the pulvinar is more important in man and the higher primates than in the subprimates.

Taken in conjunction with recent clinical observations made during stereotaxic surgery, of anomia occurring during

stimulation of the left pulvinar, the findings obtained from the present work allow the conclusion that the pulvinar acts as a subcortical speech centre.

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